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constituted by tertiary structure dependent coherent surface areas large

```
enough to accommodate antibody binding and conserved among isoallergens,
     variants, and/or homologous allergens from related species. Mutant forms
     of Bet v 1 and Ves v 5 allergens were produced. The Bet v 1 mutants
     displayed reduced IgE binding although the tertiary structure of the
     wild-type Bet v 1 allergen was retained. A "triple-patch mutant" of Bet
     1 was able to induce proliferation in T cell lines from 3 different birch
     pollen allergic patients with stimulation indexes similar to recombinant
     and naturally occurring Bet v 1.
ST
     allergy vaccine allergen mutant B cell epitope IgE binding; Bet v 1
     allergen recombinant mutant allergy vaccine; Ves v 5 allergen recombinant
     mutant allergy vaccine
ΙT
     Epitopes
        (B cell, mutation of; mutant recombinant allergens for use as allergy
        vaccines)
ΙT
    Allergens
     RL: BPN (Biosynthetic preparation); BPR (Biological process); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC
     (Process); USES (Uses)
        (Bet v I (Betula verrucosa, I); mutant recombinant allergens for use
as
        allergy vaccines)
TΤ
     Immunoglobulins
     RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
        (E, binding of, redn. of; mutant recombinant allergens for use as
        allergy vaccines)
IT
    Ant (Formicidae)
        (Formicoidae; mutant recombinant allergens for use as allergy
vaccines)
    Dicotyledon (Magnoliopsida)
        (Oleales; mutant recombinant allergens for use as allergy vaccines)
IT
    Monocotyledon (Liliopsida)
        (Poales; mutant recombinant allergens for use as allergy vaccines)
IΤ
    Allergens
     RL: BPN (Biosynthetic preparation); BPR (Biological process); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC
     (Process); USES (Uses)
        (Ves v 5 (Vespula vulgaris, V); mutant recombinant allergens for use
as
        allergy vaccines)
IT
    Animal
    Apidae
    Asterales
    Blattaria
    Cat (Felis catus)
    Dermatophagoides
    Dog (Canis familiaris)
    Fagales
    Horse (Equus caballus)
    Hymenoptera
     Pinales
    Pollen
    Urticales
    Venoms
        (allergens; mutant recombinant allergens for use as allergy
        vaccines)
IT
    Vaccines
```

```
(allergy; mutant recombinant allergens for use as allergy vaccines)
IT
     Tertiary structure
        (maintenance of; mutant recombinant allergens for use as allergy
        vaccines)
ΙT
     Allergy inhibitors
        (mutant recombinant allergens for use as allergy vaccines)
IT
     Allergens
     RL: BPN (Biosynthetic preparation); BPR (Biological process); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC
     (Process); USES (Uses)
        (mutant recombinant allergens for use as allergy vaccines)
IT
     Protein sequences
        (of Bet v 1 and Ves v 5 mutants)
                                                                 244065-84-7P
TΤ
     244065-79-0P
                    244065-81-4P
                                  244065-82-5P
                                                  244065-83-6P
                                   244065-87-0P
                                                                 244065-89-2P
                    244065-86-9P
                                                  244065-88-1P
     244065-85-8P
     244065-90-5P
     RL: BPN (Biosynthetic preparation); BPR (Biological process); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC
     (Process); USES (Uses)
        (amino acid sequence; mutant recombinant allergens for use as allergy
        vaccines)
     244179-41-7, PN: WO9947680 FIG: 3 unclaimed DNA
                                                       244179-50-8, PN:
ΙT
                                     244179-51-9, PN: WO9947680 FIG: 3
     WO9947680 FIG: 3 unclaimed DNA
     unclaimed DNA
                     244179-52-0, PN: WO9947680 FIG: 3 unclaimed DNA
     244179-54-2, PN: WO9947680 FIG: 3 unclaimed DNA
                                                       244179-56-4, PN:
     WO9947680 FIG: 3 unclaimed DNA
                                      244179-57-5, PN: WO9947680 FIG: 3
                     244179-58-6, PN: WO9947680 FIG: 3 unclaimed DNA
     unclaimed DNA
     244179-59-7, PN: WO9947680 FIG: 3 unclaimed DNA
                                                       244179-60-0, PN:
     WO9947680 FIG: 3 unclaimed DNA
                                      244179-61-1, PN: WO9947680 FIG: 3
     unclaimed DNA
                     244179-62-2, PN: WO9947680 FIG: 3 unclaimed DNA
     244179-64-4, PN: WO9947680 FIG: 13 unclaimed DNA
                                                        244179-67-7, PN:
                                       244179-68-8, PN: WO9947680 FIG: 13
     WO9947680 FIG: 13 unclaimed DNA
     unclaimed DNA
     RL: PRP (Properties)
        (unclaimed nucleotide sequence; mutant recombinant allergens for use
as
       allergy vaccines)
RE.CNT 6
(1) Ferreira, F; FASEB JOURNAL FOR EXPERIMENTAL BIOLOGY 1998, V12(2), P231
(2) Hoffman, D; JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY 1993, V92(5), P707
   MEDLINE
(3) Smith, A; CLINICAL AND EXPERIMENTAL ALLERGY 1997, V27(5), P593 CAPLUS
(4) Spangfort, M; INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY 1997,
   V113(1-3), P243 CAPLUS
(5) The Rockefeller University; WO 9733910 A 1997 CAPLUS
(6) Wiedemann, P; JOURNAL OF BIOLOGICAL CHEMISTRY 1996, V271(47), P29915
CAPLUS
     ANSWER 2 OF 2 CAPLUS COPYRIGHT 2000 ACS
L1
     1993:232158 CAPLUS
ΑN
DN
     118:232158
     Four recombinant isoforms of Cor a I, the major allergen of hazel pollen,
     show different IgE-binding properties
     Breiteneder, Heimo; Ferreira, Fatima; Hoffmann-Sommergruber, Karin;
ΑU
Ebner,
     Christof; Breitenbach, Michael; Rumpold, Helmut; Kraft, Dietrich;
```

Scheiner, Otto CS Inst. Gen. Exp. Pathol., Univ. Vienna, Vienna, A-1090, Austria Eur. J. Biochem. (1993), 212(2), 355-62 SO CODEN: EJBCAI; ISSN: 0014-2956 DTJournal English LΑ CC 15-9 (Immunochemistry) Section cross-reference(s): 3, 11 Previous studies showed that pollens from trees of the order Fagales AB (e.g. birch, alder, hazel, and hornbeam) all contain 1 major allergen. proteins are cross-reactive among these tree species , and .apprx.95% of tree-pollen-allergic patients display IgE binding to these allergens. Using the reported N-terminal amino acid sequence of the hazel pollen allergen Cor a I, it was possible to amplify Cor-.alpha.-I cDNA by use of PCR. Four clones with cDNA inserts were isolated. All 4 clones contained an open reading frame of 477 nucleotides (159 amino acids) but differed in length for their 3'-non-coding regions. Within the overlapping regions, the nucleotide sequence of the 3'-non-coding regions of the 4 clones were nearly identical. The open reading frames coded for different isoforms of the major hazel pollen allergen, Cor a I. The clones were designated Cor a I/5, 6, 11 and 16, resp. Comparison of the deduced amino acid sequences of these Cor a I isoforms revealed identities of 96-99%. The sequence identities between the Cor a I isoforms and Bet v I, the major birch pollen allergen, were 71-73% (80.5-83% similarity). Comparing amino acid sequences of Cor a I isoforms with the published sequences of Aln g I, the major allergen from alder, and Car b I and isoforms, the major allergen from hornbeam, 75.5-76.7% identity (83.6-85% similarity) and 83.6-89.9% sequence identity (89.3-95% similarity), resp., was found. The 4 Cor a I cDNAs were subcloned into plasmid pKK223-3 and expressed in Escherichia coli as non-fusion proteins; their capacity to bind serum IgE from tree-pollen-allergic patients was investigated. The 4 cloned isoforms showed an apparent mol. mass of 17 kDa in SDS/PAGE, identical to the natural, pollen-derived Cor a I. IgE antibodies from tree-pollen-allergic patients reacted with all 4 recombinant isoforms. However, marked differences were noted in the IgE-binding patterns of the distinct isoforms. Furthermore, Cor a I/11 was the only isoform recognized by the anti-(Ber v I) monoclonal antibody, BIP 1. These results demonstrate that Cor a I isoforms display different antigenic and allergenic properties, very likely due to few but significant changes in their amino acid sequences. These findings have implications for the development of reagents for diagnosis and immunotherapy for type I allergies. hazel pollen allergen isoform; Corylus major allergen I sequence TΨ Fagales (allergens of pollen of, human IgE to, hazel major allergen I isoforms reactivity for) TТ Protein sequences (for allergen I isoforms of hazel) IT Immunoglobulins RL: BIOL (Biological study) (E, to allergen I of hazel, of humans, isoform reactivity of)

```
Deoxyribonucleic acid sequences
IT
        (complementary, for allergen I isoforms of hazel)
TΤ
     Allergy
        (immediate hypersensitivity, IgE to tree pollen of humans with, hazel
        major allergen I isoform reactivity of)
     143066-17-5, Allergen Cor a I (hazel isoform 1)
                                                       143066-18-6, Allergen
TΤ
     Cor a I (hazel isoform 2) 143066-19-7, Allergen Cor a I (hazel isoform
         143066-20-0, Allergen Cor a I (hazel isoform 4)
     RL: PRP (Properties)
        (amino acid sequence of)
=> s birch allergen
           155 BIRCH ALLERGEN
L2
=> s 12 and beta v1
             0 L2 AND BETA V1
1.3
=> s 12 and epitope
            27 L2 AND EPITOPE
L4
=> dup remove 14
PROCESSING COMPLETED FOR L4
             26 DUP REMOVE L4 (1 DUPLICATE REMOVED)
=> d 15 all 1-26
     ANSWER 1 OF 26 CAPLUS COPYRIGHT 2000 ACS
L5
ΑN
     2000:469064 CAPLUS
DN
     133:191900
     Rapid production of the major birch pollen allergen Bet v 1 in Nicotiana
TI
     benthamiana plants and its immunological in vitro and in vivo
     characterization
ΑU
     Krebitz, Monika; Wiedermann, Ursula; Essl, Dagmar; Steinkellner, Herta;
     Wagner, Birgit; Turpen, Thomas H.; Ebner, Christof; Scheiner, Otto;
     Breiteneder, Heimo
     Department of Pathophysiology, University of Vienna, Vienna, 1090,
CS
Austria
     FASEB J. (2000), 14(10), 1279-1288
     CODEN: FAJOEC; ISSN: 0892-6638
     Federation of American Societies for Experimental Biology
DT
     Journal
LA
     English
CC
     15-9 (Immunochemistry)
     Type I allergies are immunol. disorders that afflict a quarter of the
AΒ
     world's population. Improved diagnosis of allergic diseases and the
     formulation of new therapeutic approaches are based on the use of
     recombinant allergens. The authors describe here for the first time the
     application of a rapid plant-based expression system for a plant-derived
     allergen and its immunol. characterization. The authors expressed the
     authors' model allergen Bet v 1, the major birch pollen allergen, in the
     tobacco-related species Nicotiana benthamiana using a tobacco mosaic
virus
```

vector. Two weeks post-inoculation, plants infected with recombinant viral RNA contg. the Bet v 1 coding sequence accumulated the allergen to levels of 200 .mu.g/g leaf material. Total non-purified protein exts. from plants were used for immunol. characterizations. IgE immunoblots and ELISA inhibition assays showed comparable IgE binding properties for tobacco recombinant (r) Bet v 1 and natural (n) Bet v 1, suggesting that the B cell epitopes were preserved when the allergen was expressed in N. benthamiana plants. Using a murine model of type I allergy, mice immunized with crude leaf exts. contg. Bet v 1 with rBet v 1 produced in E. coli or with birch pollen ext. generated comparable allergen-specific IgE and IgG1 antibody responses and pos. type I skin test reactions. These results demonstrate that non-purified Bet v 1 overexpressed in N. benthamiana has the same immunogenicity as purified Bet v 1 produced in E. coli or nBet v 1. The authors therefore conclude that this plant expression system offers a viable alternative to fermn.-based prodn. of allergens in bacteria or yeasts. In addn., there may be a broad utility of this system for the development of new and low-cost vaccination strategies against allergy. Bet v1 allergen tobacco; birch allergen Nicotiana stIT Allergens RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation) (Bet v I (Betula verrucosa, I); prepn. and immunol. characterization of birch pollen allergen from tobacco) IT Immunoglobulins RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (E; to tobacco-derived birch pollen allergen) IΤ Immunoglobulins RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (G1; to tobacco-derived birch pollen allergen) ΙT Tobacco mosaic virus (as vector for expression of birch pollen allergen in Nicotiana benthamiana) ΙT Tobacco (Nicotiana benthamiana) (prepn. and immunol. characterization of birch pollen allergen from) ITBirch (Betula) (prepn. and immunol. characterization of birch pollen allergen from tobacco) ΤТ Virus vectors (tobacco mosaic virus as vector for expression of birch pollen allergen in Nicotiana benthamiana) RE.CNT 41 (1) Arakawa, T; Transgenic Res 1997, V6, P403 CAPLUS (2) Bauer, L; Clin Exp Immunol 1997, V107, P536 CAPLUS (3) Breiteneder, H; EMBO J 1989, V88, P1935 (4) Casper, S; Gene 1996, V173, P69 CAPLUS (5) Ebner, C; Eur J Immunol 1993, V23, P1523 CAPLUS (6) Ebner, C; J Immunol 1993, V150, P1047 CAPLUS (7) Ebner, C; J Immunol 1995, V154, P1932 CAPLUS (8) Ferreira, F; J Biol Chem 1993, V268, P19574 CAPLUS (9) Ferreira, F; J Exp Med 1996, V183, P599 CAPLUS (10) Gajhede, M; Natl Struct Biol 1996, V3, P1040 CAPLUS

- (11) Godnic-Cvar, J; J Allergy Clin Immunol 1997, V99, P354 CAPLUS
- (12) Hakkart, G; Clin Exp Allergy 1998, V28, P45
- (13) Haq, T; Science 1995, V268, P714 CAPLUS
- (14) Hoffmann-Sommergruber, K; Gene 1997, V197, P91 CAPLUS
- (15) Hoffmann-Sommergruber, K; Protein Exp Purif 1997, V9, P33 CAPLUS
- (16) Hoyne, G; Int Immunol 1996, V7, P335
- (17) Huecas, S; Eur J Biochem 1999, V261, P539 CAPLUS
- (18) Ipsen, H; J Allergy Clin Immunol 1983, V72, P150 CAPLUS
- (19) Jarolim, E; Allergy 1989, V44, P385 MEDLINE
- (20) Jarolim, E; Int Arch Allergy Appl Immunol 1989, V90, P54 CAPLUS
- (21) Koo, M; Proc Natl Acad Sci USA 1999, V96, P7774 CAPLUS
- (22) Kraft, D; Allergy 1998, V53, P62 MEDLINE
- (23) Kraft, D; Int Arch Allergy Immunol 1999, V118, P171 CAPLUS
- (24) Kumagai, M; Proc Natl Acad Sci USA 1993, V90, P427 CAPLUS
- (25) Mason, H; Proc Natl Acad Sci USA 1992, V89, P11745 CAPLUS
- (26) Mason, H; Proc Natl Acad Sci USA 1996, V93, P5335 CAPLUS
- (27) McCormick, A; Proc Natl Acad Sci USA 1999, V96, P703 CAPLUS
- (28) Seymour, B; J Exp Med 1998, V187, P721 CAPLUS
- (29) Smith, P; J Allergy Clin Immunol 1996, V98, P331 CAPLUS
- (30) Sowka, S; Eur J Biochem 1998, V255, P213 CAPLUS
- (31) Sowka, S; J Biol Chem 1998, V273, P28091 CAPLUS
- (32) Swoboda, I; J Biol Chem 1995, V270, P2607 CAPLUS
- (33) Turpen, T; Bio/Technology 1995, V13, P53 CAPLUS
- (34) Vailes, L; J Allergy Clin Immunol 1998, V101, P274 CAPLUS
- (35) Valenta, R; Curr Opin Immunol 1995, V7, P751 CAPLUS
- (36) Vrtala, S; J Clin Invest 1997, V99, P1673 CAPLUS
- (37) Wen, J; Mol Phyl Evol 1997, V8, P317 CAPLUS
- (38) Wiedermann, U; Clin Exp Immunol 1998, V111, P144 CAPLUS
- (39) Wiedermann, U; Int Immunol 1999, V11, P1131 CAPLUS
- (40) Wiedermann, U; J Allergy Clin Immunol 1999, V103, P1202 CAPLUS
- (41) Yasue, M; Cell Immunol 1997, V181, P30 CAPLUS
- L5 ANSWER 2 OF 26 MEDLINE
- AN 1999384123 MEDLINE
- DN 99384123
- TI Blocking antibodies induced by specific allergy vaccination prevent the activation of CD4+ T cells by inhibiting serum-IgE-facilitated allergen presentation.
- AU van Neerven R J; Wikborg T; Lund G; Jacobsen B; Brinch-Nielsen A; Arnved J; Ipsen H
- CS ALK-Abello, Horsholm, Denmark; and Lung and Allergy Clinic, Copenhagen, Denmark.. joost-vanneerven@tanox.nl
- SO JOURNAL OF IMMUNOLOGY, (1999 Sep 1) 163 (5) 2944-52. Journal code: IFB. ISSN: 0022-1767.
- CY United States
- DT Journal; Article; (JOURNAL ARTICLE)
- LA English
- FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
- EM 199911
- EW 19991104
- Allergen-specific CD4+ T lymphocytes are activated at extremely low allergen concentrations in vivo as a result of serum-facilitated allergen presentation (S-FAP). It is not clear at present if specific allergy vaccination (SAV) has an effect on this mechanism. Here we show that birch allergen-specific serum-IgE facilitates the presentation of Bet v 1, the major birch pollen allergen, to Bet v 1-specific CD4+ T lymphocytes by a factor of >100. This process is CD23 mediated, could be detected in sera from the majority of birch-allergic

```
patients, and was clearly dose dependent. S-FAP of Bet v 1 was inhibited
     in patients undergoing long-term birch SAV, but not by sera from patients
     undergoing grass SAV, indicating that birch-specific Abs are involved.
     This resulted in decreased proliferation and IL-4, IL-5, IL-10, and
     IFN-gamma production of Bet v 1-specific T cells. The inhibition was
     already noted after 3-9 mo of SAV and could not be solely explained by
     increased serum levels of birch-specific IgG4. When IgG- and
     IgA/IgM-containing fractions of long-term SAV sera were used to inhibit
     S-FAP, only IgG-containing fractions were shown to inhibit S-FAP. These
     results indicate that blocking IgG Abs induced by SAV inhibits the
     occurrence of S-FAP at very low allergen concentrations, resulting in
     significantly higher allergen threshold levels to obtain T cell
     proliferation and cytokine production and thus allergen-induced
late-phase
     responses.
CT
     Check Tags: Human
     *Allergens: IM, immunology
      Allergens: ME, metabolism
      Antibodies, Anti-Idiotypic: PH, physiology
     *Antibodies, Blocking: BI, biosynthesis
     *Antibodies, Blocking: PH, physiology
     *Antigen Presentation: IM, immunology
      Antigens, CD19: IM, immunology
      Body Temperature
      Cells, Cultured
     *CD4-Positive T-Lymphocytes: IM, immunology
      CD4-Positive T-Lymphocytes: ME, metabolism
      Desensitization, Immunologic
      Epitopes, T-Lymphocyte: IM, immunology
     *IgE: BL, blood
      IgE: IM, immunology
      IgE: PH, physiology
      IgG: BL, blood
      IgG: IM, immunology
      Immune Sera: PH, physiology
     *Lymphocyte Transformation: IM, immunology
     *Plant Proteins: IM, immunology
      Plant Proteins: ME, metabolism
      Receptors, IgE: IM, immunology
      Trees: IM, immunology
     126161-14-6 (BetvI protein); 37341-29-0 (IgE)
     0 (anti-IgE); 0 (anti-IgG); 0 (Allergens); 0 (Antibodies,
Anti-Idiotypic);
     0 (Antibodies, Blocking); 0 (Antigens, CD19); 0 (Epitopes,
     T-Lymphocyte); 0 (IgG); 0 (Immune Sera); 0 (Plant Proteins); 0
(Receptors,
     IgE)
    ANSWER 3 OF 26 CAPLUS COPYRIGHT 2000 ACS
ΑN
     1999:273002 CAPLUS
DN
     131:115196
     Identification of a highly promiscuous and an HLA allele-specific T-cell
     epitope in the birch major allergen Bet v 1: HLA restriction,
     epitope mapping and TCR sequence comparisons
AU
     Friedl-Hajek, R.; Spangfort, M. D.; Schou, C.; Breiteneder, H.; Yssel,
H.;
     Van Neerven, R. J. Joost
CS
     Department of General and Experimental Pathology, Vienna, Austria
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SO
     Clin. Exp. Allergy (1999), 29(4), 478-487
     CODEN: CLEAEN; ISSN: 0954-7894
PB
     Blackwell Science Ltd.
DT
     Journal
LА
     English
CC
     15-9 (Immunochemistry)
     Section cross-reference(s): 3
AΒ
     Background: allergen-specific CD4+ T cells play an important regulatory
     role in atopic allergy. Objective: to investigate the human leukocyte
     antigen (HLA) restriction and T-cell receptor (TCR) usage of
     allergen-specific T-cell clones (TCCs) that react with defined
     epitopes of Bet v 1, the major birch pollen allergen. Methods:
     five Bet v 1-specific TCCs derived from two birch pollen-allergic
     individuals and specific for Bet v 1, were epitope-mapped with
     overlapping synthetic peptides. In addn., HLA-restriction and TCR CDR3
     sequences were detd. Results: three TCCs reacted with a Bet v 1 peptide
     contg. amino acid residues 21-33 (BP21), the other two TCCs reacted with
     minimal peptide comprising residues 37-45 (BP37). Studies using
     neutralizing anti-HLA-monoclonal antibodies and HLA-typed APCs showed
that
     the BP37-specific TCCs were restricted by a HLA-DQA1*0301/DQB1*0603
     heterodimer. In contrast, BP21 was recognized in a highly promiscuous
     manner. TCCs recognizing this sequence were restricted by HLA-DPB1*0201,
     a HLA-DQA1*0201/DQB1*0201 heterodimer, or HLA-DRB3*0101. Reverse
     transcription-polymerase chain reaction with primers for all known TCRAV
     and TCRBV gene segments, followed by CDR3 region sequencing, revealed the
     usage of five different TCRAV and four different TCRBV gene segments by
     the TCCs, as well as diversity in the joining region. All BP21-specific
     TCCs contained a neq. charged residue in their CDR3.alpha. regions, the
     CDR3.beta. regions showed a high concn. of polar and OH-group bearing
     residues. BP37-specific TCCs shared the amino acid combination LY in the
     middle of their CDR3.alpha. regions, the CDR3.beta. regions showed high
     concn. of OH-group bearing or charged residues. Conclusions: this study
     shows the existence of a highly promiscuous T-cell epitope in
     Bet v 1. The presence of addnl. T-cell epitopes in Bet v 1 may,
     however, hamper the clin. applicability of the epitope.
     Likewise, the diversity in TCR usage by T cells recognizing the
     epitope does not support the development of TCR-directed
     immunotherapy for birch pollen allergy.
     birch allergen Betv1 T cell epitope HLA
     restriction; TCR receptor cDNA sequence birch allergen
     human
     Allergens
     RL: ADV (Adverse effect, including toxicity); BOC (Biological
     PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
        (Bet v 1 (Betula verrucosa, 1); highly promiscuous and human HLA
        allele-specific T-cell epitope in birch major allergen Bet v
        1 and HLA restriction, epitope mapping and TCR sequence
        comparisons)
IT
     Histocompatibility antigens
     RL: ADV (Adverse effect, including toxicity); BPR (Biological process);
     BIOL (Biological study); PROC (Process)
        (HLA-DP; highly promiscuous and human HLA allele-specific T-cell
      epitope in birch major allergen Bet v 1 and HLA restriction,
      epitope mapping and TCR sequence comparisons)
IΤ
     Gene, animal
```

```
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU
     (Occurrence)
        (HLA-DPB1; highly promiscuous and human HLA allele-specific T-cell
     epitope in birch major allergen Bet v 1 and HLA restriction,
     epitope mapping and TCR sequence comparisons)
IT
    Histocompatibility antigens
    RL: ADV (Adverse effect, including toxicity); BPR (Biological process);
    BIOL (Biological study); PROC (Process)
        (HLA-DQ; highly promiscuous and human HLA allele-specific T-cell
     epitope in birch major allergen Bet v 1 and HLA restriction,
     epitope mapping and TCR sequence comparisons)
ΙT
    Gene, animal
    RL: BOC (Biological occurrence); BIOL (Biological study); OCCU
     (Occurrence)
        (HLA-DQA1; highly promiscuous and human HLA allele-specific T-cell
     epitope in birch major allergen Bet v 1 and HLA restriction,
     epitope mapping and TCR sequence comparisons)
ΙT
    Gene, animal
    RL: BOC (Biological occurrence); BIOL (Biological study); OCCU
     (Occurrence)
        (HLA-DQB1; highly promiscuous and human HLA allele-specific T-cell
     epitope in birch major allergen Bet v 1 and HLA restriction,
     epitope mapping and TCR sequence comparisons)
ΙT
    Histocompatibility antigens
    RL: ADV (Adverse effect, including toxicity); BPR (Biological process);
    BIOL (Biological study); PROC (Process)
        (HLA-DR; highly promiscuous and human HLA allele-specific T-cell
     epitope in birch major allergen Bet v 1 and HLA restriction,
     epitope mapping and TCR sequence comparisons)
IT
    Gene, animal
    RL: BOC (Biological occurrence); BIOL (Biological study); OCCU
     (Occurrence)
        (HLA-DRB3; highly promiscuous and human HLA allele-specific T-cell
     epitope in birch major allergen Bet v 1 and HLA restriction,
     epitope mapping and TCR sequence comparisons)
TI
        (atopy; highly promiscuous and human HLA allele-specific T-cell
     epitope in birch major allergen Bet v 1 and HLA restriction,
     epitope mapping and TCR sequence comparisons)
    Peptides, biological studies
    RL: ADV (Adverse effect, including toxicity); BOC (Biological
    PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
        (epitope; highly promiscuous and human HLA allele-specific
        T-cell epitope in birch major allergen Bet v 1 and HLA
        restriction, epitope mapping and TCR sequence comparisons)
    Alleles
    Birch (Betula pendula)
    CD4-positive T cell
    MHC restriction
    Protein sequences
    cDNA sequences
        (highly promiscuous and human HLA allele-specific T-cell
     epitope in birch major allergen Bet v 1 and HLA restriction,
     epitope mapping and TCR sequence comparisons)
IT
    Gene, animal
    TCR .alpha..beta. (receptor)
    RL: BOC (Biological occurrence); PRP (Properties); BIOL (Biological
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study); OCCU (Occurrence)
        (highly promiscuous and human HLA allele-specific T-cell
      epitope in birch major allergen Bet v 1 and HLA restriction,
      epitope mapping and TCR sequence comparisons)
ΙT
     Epitopes
        (mapping; highly promiscuous and human HLA allele-specific T-cell
      epitope in birch major allergen Bet v 1 and HLA restriction,
      epitope mapping and TCR sequence comparisons)
IT
     Epitopes
        (peptide; highly promiscuous and human HLA allele-specific T-cell
      epitope in birch major allergen Bet v 1 and HLA restriction,
      epitope mapping and TCR sequence comparisons)
     232260-84-3
                  232260-85-4
     RL: ADV (Adverse effect, including toxicity); BOC (Biological
occurrence);
     PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
        (epitope; highly promiscuous and human HLA allele-specific
        T-cell epitope in birch major allergen Bet v 1 and HLA
        restriction, epitope mapping and TCR sequence comparisons)
     199415-74-2, GenBank Y15198 199415-75-3, GenBank Y15199
                                                                199415-76-4,
     GenBank Y15200
                     199415-77-5, GenBank Y15201 199415-78-6, GenBank
Y15202
     199415-79-7, GenBank Y15203
                                   199415-80-0, GenBank Y15204
                                                                 199415-81-1,
     GenBank Y15205
                      199415-82-2, GenBank Y15206
                                                    199415-83-3, GenBank
Y15207
    RL: PRP (Properties)
        (nucleotide sequence; highly promiscuous and human HLA allele-specific
        T-cell epitope in birch major allergen Bet v 1 and HLA
        restriction, epitope mapping and TCR sequence comparisons)
RE.CNT
(1) Bowness, P; Eur J Immunol 1993, V23, P1417 CAPLUS
(2) Breiteneder, H; EMBO J 1989, V8, P1935 CAPLUS
(3) Breiteneder, H; Eur J Biochem 1993, V552, P1
(4) Breiteneder, H; Immunogenetics 1995, V42, P53 CAPLUS
(5) Breiteneder, H; J Allergy Clin Immunol 1992, V90, P909 MEDLINE
(6) Brown, L; Int Immunol 1991, V3, P1307 MEDLINE
(7) Davies, M; Nature 1988, V334, P395
(8) de Campos-Lima, P; J Exp Med 1997, V186, P83 CAPLUS
(9) Del Simonian, H; J Exp Med 1993, V177, P1623
(10) Durham, S; J Immunol 1992, V148, P2390 CAPLUS
(11) Gajhede, M; Nature Struct Biol 1996, V3, P1040 CAPLUS
(12) Garcia, K; An ab T cell receptor structure at 2.5 A and its orientation
    the TCR-MHC complex Sci 1996, V274, P209 CAPLUS
(13) Hamid, Q; J Allergy Clin Immunol 1997, V99, P254 CAPLUS
(14) Henwood, J; Eur J Immunol 1993, V23, P1256 CAPLUS
(15) Ipsen, H; Clin Exp Allergy 1992, V22, P391 MEDLINE
(16) Ipsen, H; J Allergy Clin Immunol 1983, V72, P150 CAPLUS
(17) Jutel, M; J Immunol 1995, V154, P4187 CAPLUS
(18) Kay, A; J Exp Med 1991, V173, P775 CAPLUS
(19) Lannes-Viera, J; Eur J Immunol 1995, V25, P611 MEDLINE
(20) Larsen, J; Mol Immunol 1992, V29, P703 CAPLUS
(21) Marsh, S; Tissue Antigens 1995, V45, P258
(22) May, E; Int Immunol 1996, V8, P1815 CAPLUS
(23) Meinl, E; J Clin Invest 1993, V92, P2633 CAPLUS
(24) Moss, P; Immunogenetics 1995, V42, P10 CAPLUS
(25) Moss, P; Proc Natl Acad Sci USA 1991, V88, P8987 CAPLUS
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- (26) Robinson, D; N Engl J Med 1992, V326, P298 MEDLINE
- (27) Rock, E; J Exp Med 1994, V79, P323
- (28) Secrist, H; J Exp Med 1993, V178, P2123 CAPLUS
- (29) Struyk, L; Hum Immunol 1995, V44, P220 CAPLUS
- (30) van Neerven, R; Clin exp Allergy 1998, V28, P423 CAPLUS
- (31) van Neerven, R; Immunol Today 1996, V17, P526 MEDLINE
- (32) van de Vijver, C; Eur J Immunol 1995, V25, P958
- (33) Varney, V; J Clin Invest 1993, V92, P644 MEDLINE
- (34) Wedderburn, L; Proc Natl Acad Sci USA 1993, V90, P8214 CAPLUS
- (35) Wierenga, E; J Immunol 1990, V144, P4651 MEDLINE
- L5 ANSWER 4 OF 26 BIOSIS COPYRIGHT 2000 BIOSIS
- AN 2000:9412 BIOSIS
- DN PREV20000009412
- TI Pollen-related food allergy: Cloning and immunological analysis of isoforms and mutants of Mal d 1, the major apple allergen, and Bet v 1, the major birch pollen allergen.
- AU Son, D. Y.; Scheurer, S.; Hoffmann, A.; Haustein, D.; Vieths, S. (1)
- CS (1) Department of Allergology, Paul-Ehrlich-Institut, Paul-Ehrlich-Str. 51-59, D-63225, Langen Germany
- SO European Journal of Nutrition, (Aug., 1999) Vol. 38, No. 4, pp. 201-215. ISSN: 1436-6207.
- DT Article
- LA English
- SL English
- AB Background: Mal d 1, the major apple allergen, cross-reacts with IgE specific for the major birch pollen allergen, Bet v 1, and is responsible for birch pollen related food allergy to apple. Isoforms of Bet v 1 showing minor sequence variations display different binding capacity for specific IgE antibodies from allergic patients. Moreover,

## strain-dependent

variation of allergenicity has been reported for apples. Objective: To investigate the occurrence of strain-dependent isoforms of Mal d 1 which may differ in their allergenic potential, to obtain data on structures essential for binding of Mal d 1 to the antibody, and to gain insights into the structures responsible for its IgE cross-reactivity to Bet v 1. Methods: The cDNA of Mal d 1 from various apple strains was amplified by

PCR strategy based on conserved regions of known Mal d 1-sequences, and sequenced. Two major isoforms of Mal d 1 were expressed as recombinant proteins and purified, as were different variants of the major b irch pollen allergen, Bet v 1. Together with already existing recombinant

## birch

pollen and apple allergens, these were subjected to allergenicity testing by IgE-immunoblotting, enzyme allergo sorbent test and dose related mediator release. "Hot-spots" for IgE-reactivity were identified by site-directed mutagenesis. Results: Twelve Mal d 1-clones were sequenced from 7 apple varieties and compared to 3 known Mal d 1 sequences. The clones were clustered into two groups, each showing a high degree of sequence identity to one of the known sequences and specific differences to the third sequence. No strain-specific sequences were identified. In contrast, apple strains with reported differences in allergenicity showed different expression levels of the major allergen. Immunologic testing of recombinant allergens revealed high IgE binding capacity of 2 major isoforms, named GD26 and GS29, with a slightly higher IgE binding capacity

of GD26. Moreover, the allergenicity was similar to another rM al d 1 reported in the literature, representing the isoform divergent from our

clones. Mutational analysis of our Mal d 1 allergens identified serine in position 111 as essential for IgE binding. Allergenicity was almost depleted by changing this residue into a proline. Moreover, the corresponding serine residue, present in position 112 of Bet v 1, was in similar manner crucial for the allergenicity of the birch pollen allergen. Conclusion: We conclude that divergent allergenicity of apple strains mainly depends on different expression levels of the major allergen. Introduction of a proline residue in position 111 of Mal d 1 and in position 112 of Bet v 1 led to a drastic reduction of allergenicity of both the pollen and the food allergen, obviously also removing the cross-reactive epitope. Mutants with reduced IgE-reactivity but maintained T-cell reactivity may represent new candidates for a safer specific immunotherapy with reduced side-effects. CC Nutrition - General Studies, Nutritional Status and Methods \*13202 Genetics and Cytogenetics - General \*03502 Biochemical Studies - General \*10060 Immunology and Immunochemistry - General; Methods \*34502 \*35500 Allergy Food Technology - General; Methods \*13502 Biophysics - General Biophysical Studies \*10502 BC Hominidae 86215 IT Major Concepts Molecular Genetics (Biochemistry and Molecular Biophysics); Immune System (Chemical Coordination and Homeostasis); Foods; Nutrition IT Chemicals & Biochemicals Bet v 1: allergen, expression, immunological analysis, major birch allergen, molecular cloning; IgE [immunoqlobulin E]; Mal d 1: allergen, expression, immunological analysis, major apple allergen, molecular cloning IT Methods & Equipment PCR [polymerase chain reaction]: DNA amplification method; SDS-PAGE [SDS-polyacrylamide gel electrophoresis]: separation method; Western blotting: detection method; site-directed mutagenesis: genetic method Miscellaneous Descriptors food allergy: pollen-related ORGN Super Taxa Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia; Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia ORGN Organism Name BALB/c mouse (Muridae); human (Hominidae): patient ORGN Organism Superterms Animals; Chordates; Humans; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Primates; Rodents; Vertebrates ANSWER 5 OF 26 CAPLUS COPYRIGHT 2000 ACS L5 1997:232478 CAPLUS ΆN DN 126:304872 ΤI Conversion of the major birch pollen allergen, Bet v 1, into two nonanaphylactic Txcell epitope-containing fragments. Candidates for a novel form of specific immunotherapy ΑU Vrtala, Susanne; Hirtenlehner, Kora; Vangelista, Luca; Pastore, Annalisa;

Eichler, Hans-Georg; Sperr, Wolfgang R.; Valent, Peter; Ebner, Christof;

Department of Immunopathology, Institute of General and Experimental

Pathology, AKH, University of Vienna, Vienna, A-1090, Austria

Kraft, Dietrich; Valenta, Rudolf

CS

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J. Clin. Invest. (1997), 99(7), 1673-1681
     CODEN: JCINAO; ISSN: 0021-9738
PB
     Rockefeller University Press
DT
     Journal
LA
     English
     15-9 (Immunochemistry)
     A novel approach to reduce the anaphylactic activity of allergens is
AΒ
     suggested. The strategy makes use of the presence of conformational IqE
     epitopes on one of the most common allergens. The three
     dimensional structure of the major birch pollen allergen, Bet v 1, was
     disrupted by expressing two parts of the Bet v 1 cDNA representing amino
     acids 1-74 and 75-160 in Escherichia coli. In contrast to the complete
     recombinant Bet v 1, the fragments showed almost no allergenicity and
     exhibited random coil conformation as analyzed by CD. Both
     nonanaphylactic fragments induced proliferation of human Bet v 1-specific
     T cell clones, indicating that they harbored all dominant T cell
     epitopes and therefore may be considered as a basis for the
     development of a safe and specific T cell immunotherapy.
    birch allergen conversion anaphylactic activity;
     immunotherapy allergen conversion T cell epitope
IT
     Allergens
     RL: BAC (Biological activity or effector, except adverse); BPN
     (Biosynthetic preparation); RCT (Reactant); BIOL (Biological study); PREP
     (Preparation)
        (Bet v I (Betula verrucosa, I), recombinant fragments; conversion of
        the major birch pollen allergen, Bet v 1, into two nonanaphylactic T
        cell epitope-contg. fragments and specific immunotherapy)
IΤ
     Anaphylaxis
     Conformation
     Immunotherapy
        (conversion of the major birch pollen allergen, Bet v 1, into two
        nonanaphylactic T cell epitope-contq. fragments and specific
        immunotherapy)
IT
     T cell (lymphocyte)
        (epitope; conversion of the major birch pollen allergen, Bet
        v 1, into two nonanaphylactic T cell epitope-contg. fragments
        and specific immunotherapy)
IT
     RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
        (epitopes; conversion of the major birch pollen allergen, Bet
        v 1, into two nonanaphylactic T cell epitope-contq. fragments
        and specific immunotherapy)
L5
    ANSWER 6 OF 26 CAPLUS COPYRIGHT 2000 ACS
ΑN
    1997:568660 CAPLUS
DN
     127:247038
    Crossreactivity and T-cell epitope specificity of Bet v
     1-specific T cells suggest the involvement of multiple isoallergens in
     sensitization to birch pollen
AU
     Sparholt, S. H.; Larsen, J. N.; Ipsen, H.; Schou, C.; Van Neerven, R. J.
    J.
CS
    ALK ABELLO, Horsholm, DK-2970, Den.
    Clin. Exp. Allergy (1997), 27(8), 932-941
    CODEN: CLEAEN; ISSN: 0954-7894
PB
    Blackwell
DT
    Journal
LΑ
    English
CC
    15-9 (Immunochemistry)
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Allergen-specific T lymphocytes play an important role in the
     pathophysiol. of atopic disease. Detailed studies of their
     epitope-specificity and crossreactivity are required for the
     development of novel approaches for specific immunotherapy. The aim of
     the study was to characterize the fine specificity of Bet v 1-specific T
     cells from allergic donors. Polyclonal T-cell lines (TCL) and T-cell
     clones (TCC), specific for Bet v 1, the major birch (Betula verrucosa)
     pollen allergen, were isolated from the peripheral blood of three
     birch-allergic patients. Their epitope-specificity was studied
     using overlapping synthetic peptides, and crossreactivity with other tree
     pollen allergens of the Fagales order was evaluated. In addn., the Bet v
     1-specific TCC were studied for their phenotype and cytokine prodn. All
     isolated Bet v 1-specific TCC (19/21 CD4+, 2/21 CD8+) reacted with
     affinity purified Bet v 1, but showed different reactivities with
     recombinant Bet v 1 (rBet v 1), and with group 1 allergens from other
     Fagales species. Epitope mapping of rBet v 1-reactive TCC with
     synthetic peptides of Bet v 1 showed the presence of four T-cell
     epitopes. Polyclonal T-cell lines reacted with 13 different
     peptides, and displayed even broader crossreactivity with group 1 pollen
     allergens from other Fagales members. This study demonstrates that apart
     from T-cell epitopes of rBet v 1, many other crossreactive or
     Bet v 1 isoallergen-specific epitopes exist. This indicates
     that isoallergenic variation plays an important role in the induction of
     Bet v 1-specific and crossreactive T-cell responsiveness to allergens.
     T cell epitope specificity Betula allergen; birch
ST
     allergen T cell crossreactivity
IT
     Allergens
     RL: BAC (Biological activity or effector, except adverse); PRP
     (Properties); BIOL (Biological study)
        (Bet v I (Betula verrucosa, I); crossreactivity and epitope
        specificity of human T-cells to birch pollen allergen)
IT
     Alder (Alnus glutinosa)
     Birch (Betula pendula)
     CD4-positive T cell
     CD8-positive T cell
     Carpinus betulus
     Epitopes
     Fagales
     Hazel (Corylus avellana)
     Oak (Quercus alba)
        (crossreactivity and epitope specificity of human T-cells to
        birch pollen allergen)
IT
     Peptides, biological studies
     RL: BAC (Biological activity or effector, except adverse); PRP
     (Properties); BIOL (Biological study)
        (crossreactivity and epitope specificity of human T-cells to
        birch pollen allergen)
     195702-59-1
                   195702-63-7
                                 195702-66-0
                                               195702-68-2
                                                             195702-71-7
     195702-74-0
                   195702-76-2
                                 195702-78-4
                                               195702-80-8
                                                             195702-82-0
     195702-85-3
                   195702-87-5
                                 195702-89-7
     RL: BAC (Biological activity or effector, except adverse); PRP
     (Properties); BIOL (Biological study)
        (crossreactivity and epitope specificity of human T-cells to
        birch pollen allergen)
L5
     ANSWER 7 OF 26 CAPLUS COPYRIGHT 2000 ACS
AN
     1997:228346 CAPLUS
DN
     126:249944
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Modulation of the allergic immune response in BALB/c mice by subcutaneous
     injection of high doses of the dominant T cell epitope from the
     major birch pollen allergen Bet v 1
ΑU
     Bauer, L.; Bohle, B.; Jahn-Schmid, B.; Wiedermann, U.; Daser, A.; Renz,
     H.; Kraft, D.; Ebner, C.
     Institute of General and Experimental Pathology, AKH, University of
CS
     Vienna, Vienna, A-1090, Austria
SO
     Clin. Exp. Immunol. (1997), 107(3), 536-541
     CODEN: CEXIAL; ISSN: 0009-9104
PB
     Blackwell
DT
     Journal
LΑ
     English
CC
     15-2 (Immunochemistry)
     Several in vitro and in vivo studies indicate that application of high
AΒ
     doses of dominant T cell epitopes can induce a state of
     antigen-specific non-responsiveness (anergy). Here, the authors
developed
     a murine model of an allergic immune response to Bet v 1, the major birch
     pollen allergen. Mice were sensitized by injection of rBet v 1 and the
     allergic state was proven by the presence of allergen-specific IgE and
     pos. immediate-type skin tests to Bet v 1. In epitope mapping
     expts., an immunodominant T cell epitope of Bet v 1 in BALB/c
     mice was identified by the use of overlapping peptides.
                                                              This peptide (BV
     139) was subsequently employed for treatment. Two tolerization protocols
     were used: in one approach, the peptide was administered to naive mice
     before immunization (group BV 139-S), in the second, already sensitized
     mice were treated (S-BV 139). The results demonstrated that
administering
     high doses of the dominant T cell epitope of Bet v 1 profoundly
     diminished T cell proliferation to the peptide in the BV 139-S group, and
     to the peptide as well as to the whole protein in the S-BV 139 group.
     Skin test reactivity to Bet v 1 was reduced in the BV 139-S group.
     However, no differences in terms of specific antibody prodn. between
     treated and untreated mice could be obsd. Thus, administration of
     dominant T cell epitopes can down-regulate the allergen-specific
     T cell response. Proceeding on the assumption that the T lymphocyte
     response to allergens is crucial for the induction and maintenance of the
     allergic disease, a modulation of the immune response to allergens by
     treatment with T cell epitope peptides could represent a
     promising concept for immunotherapy in the future.
ST
     allergy T cell epitope birch allergen;
     pollen allergen Betv1 T cell epitope
IT
     Allergens
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (Bet v I (Betula verrucosa, I); allergic immune response modulation by
        s.c. injection of high doses of dominant T cell epitope from
        major birch pollen allergen Bet v 1 in relation to immunotherapy)
ΙT
     Epitopes
     Immune tolerance
     Immunotherapy
     Pollen
     T cell (lymphocyte)
        (allergic immune response modulation by s.c. injection of high doses
of
       dominant T cell epitope from major birch pollen allergen Bet
        v 1 in relation to immunotherapy)
    Hypersensitivity
```

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(immediate hypersensitivity; allergic immune response modulation by
        s.c. injection of high doses of dominant T cell epitope from
        major birch pollen allergen Bet v 1 in relation to immunotherapy)
ΙT
     188724-41-6
     RL: BAC (Biological activity or effector, except adverse); PRP
     (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (allergic immune response modulation by s.c. injection of high doses
of
        dominant T cell epitope from major birch pollen allergen Bet
        v 1 in relation to immunotherapy)
     ANSWER 8 OF 26 CAPLUS COPYRIGHT 2000 ACS
ΑN
     1998:12536 CAPLUS
DN
     128:87790
ΤI
     Epitope analysis of birch pollen allergen in Japanese subjects
ΑU
     Abe, Yusuke; Kimura, Shoji; Kokubo, Taku; Mizumoto, Keiko; Uehara,
     Motoharu; Katagiri, Makoto
     Department of Pathology, Asahikawa Medical College, Asahikawa, 078, Japan
     J. Clin. Immunol. (1997), 17(6), 485-493
     CODEN: JCIMDO; ISSN: 0271-9142
PΒ
     Plenum Publishing Corp.
DT
     Journal
LA
     English
CC
     15-9 (Immunochemistry)
AB
     Birch pollen is a very common cause of nasal allergy (pollinosis) not
only
     in Scandinavia, Europe, Canada, and the northern part of the United
States
     but also in Hokkaido, Japan. The authors have previously reported a pos.
     assocn. between the HLA-DR9 phenotype and the development of birch pollen
     allergy in Japanese subjects. However, there is little information about
     T cell epitopes of birch pollen which are presented by HLA class
     II mols. other than HLA-DR9. Therefore, the authors analyzed the
     difference in T cell epitope usage in patients who had HLA-DR9
     vs. those who did not. Seven Japanese patients with birch pollinosis
were
     studied. Some groups of peptides representing T cell epitopes
     (Betula verrucosa; Bet VI peptides, p7-33, p23-46, p138-160) appeared to
     be shared by the majority, while another peptide (Bet VI p72-95) was
     recognized predominantly by patients who expressed HLA-DR9 and/or HLA-DQ3
    mols. Moreover, seven T cell clones and eight T cell lines were
     from two patients who did not have HLA-DR9 or HLA-DQ3. Using some of
     these T cell clones/lines, the authors investigated the relation between
     HLA class II mols. and antigenic peptides. One of these T cell clones
     recognized antigenic peptides in the context of the HLA-DQ1 mol. To the
     authors' knowledge, this is the first indication that the epitope
    on Bet VI can be presented by the HLA-DQ mol.
ST
    epitope birch allergen HLA DQ
    Allergens
    RL: PRP (Properties)
        (Bet v I (Betula verrucosa, I); epitope anal. of birch tree
        allergen in Japanese humans with pollinosis)
    HLA-DQ antigen
IT
    RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
        (HLA-DQ1 antigen; epitope anal. of birch tree allergen in
        Japanese humans with pollinosis)
    Epitope mapping
IT
```

```
Epitopes
     Hay fever
     Pollen
     T cell (lymphocyte)
        (epitope anal. of birch tree allergen in Japanese humans with
        pollinosis)
ΙT
     Peptides, biological studies
     RL: BAC (Biological activity or effector, except adverse); PRP
     (Properties); BIOL (Biological study)
        (epitope anal. of birch tree allergen in Japanese humans with
        pollinosis)
ΙT
     T cell stimulating structure-activity relationship
        (of peptides of birch pollen allergen)
ΙT
     201009-61-2
                   201009-62-3
                                 201009-63-4
                                               201009-64-5
                                                             201009-65-6
     201009-66-7
                   201009-67-8
                                                             201009-70-3
                                 201009-68-9
                                               201009-69-0
                                 201009-73-6
     201009-71-4
                   201009-72-5
                                               201009-74-7
                                                             201009-75-8
                                 201009-78-1
     201009-76-9
                   201009-77-0
                                                             201009-80-5
                                               201009-79-2
     201009-81-6
                   201009-82-7
                                 201009-83-8
                                               201009-84-9
                                                             201009-85-0
                   201009-87-2
     201009-86-1
                                 201009-88-3
                                               201009-89-4
                                                             201009-90-7
     201009-91-8
                   201009-92-9
                                 201009-93-0
     RL: BAC (Biological activity or effector, except adverse); PRP
     (Properties); BIOL (Biological study)
        (epitope anal. of birch tree allergen in Japanese humans with
        pollinosis)
L_5
    ANSWER 9 OF 26 CAPLUS COPYRIGHT 2000 ACS
AN
     1997:221926 CAPLUS
DN
     126:237360
TI
     Immunologic characterization of monoclonal antibodies that modulate human
     IgE binding to the major birch pollen allergen Bet v 1
ΑU
     Lebecque, Serge; Dolecek, Christiane; Laffer, Sylvia; Visco, Vincenzo;
     Denepoux, Stephane; Pin, Jean-Jacques; Guret, Christiane;
Boltz-Nitulescu,
     George; Weyer, Anne; Valenta, Rudolf
CS
     Laboratory for Immunlological Research, Schering-Plough, Dardilly, 69571,
SO
     J. Allergy Clin. Immunol. (1997), 99(3), 374-384
    CODEN: JACIBY; ISSN: 0091-6749
PB
    Mosby-Year Book
DT
    Journal
LΑ
    English
CC
     15-9 (Immunochemistry)
    Bet v 1 and homologous proteins represent major allergens for almost 95\%
AB
     of patients allergic to tree pollen and approx. 70% of those allergic to
     fruits and vegetables. As yet, no continuous (sequential) IqE
     epitopes have been detd. for Bet v 1, and evidence has accumulated
     that Bet v 1 IgE epitopes belong to the conformational
     (discontinuous) type. A panel of 85 mouse monoclonal anti-Bet v 1
     antibodies was raised as a tool with which to study the interaction of
    human IgE antibodies with Bet v 1. The epitopes of selected
    monoclonal antibodies (mAbs) were characterized by mapping with synthetic
    overlapping peptides and by cross-competition expts. Cross-reactivity of
    Bet v 1-specific mAbs with tree and plant food allergens was investigated
    by Western blotting. The influence of Bet v 1-specific mAbs on the
    IgE-Bet\ v\ 1 interaction was studied by competition assays with
immobilized
    purified recombinant Bet v 1 and by basophil histamine release expts.
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Antibodies that increased the IgE binding to Bet v 1 up to fivefold could

be defined, whereas others inhibited IgE binding to Bet  $v\ 1$  up to 99% and competed with the Bet v 1-induced histamine release from patients' basophils. The activity of the enhancing antibodies is interpreted as a stabilization of Bet v 1 state/IgE epitopes, which are either more accessible for certain IgE antibodies or are recognized with higher affinity. Those mAbs that competed with the Bet v 1-IgE interaction, if humanized or produced as recombinant antibody fragments, might be considered as potential tools for local allergy therapy. monoclonal antibody allergen Bet v1 IgE Allergens RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (Bet v I (Betula verrucosa, I); effect of monoclonal antibodies on the binding of human IgE to birch allergen Bet v 1) Monoclonal antibodies RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study) (effect of monoclonal antibodies on the binding of human IgE to birch allergen Bet v 1) IgE RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (effect of monoclonal antibodies on the binding of human IgE to birch allergen Bet v 1) Basophil (effect of monoclonal antibodies on the binding of human IgE to birch allergen Bet v 1 in relation to histamine release from basophils) 51-45-6, Histamine, biological studies RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (effect of monoclonal antibodies on the binding of human IgE to  $\mbox{\sc birch}$  allergen Bet v 1 in relation to histamine release from basophils) ANSWER 10 OF 26 CAPLUS COPYRIGHT 2000 ACS 1997:282897 CAPLUS 126:329438 Bip 1, a monoclonal antibody with specificity for the major birch pollen allergen Bet v 1, modulates IqE binding to the allergen Laffer, Sylvia; Vangelista, Luca; Steinberger, Peter; Kraft, Dietrich; Pastore, Annalisa; Valenta, Rudolf Institute of General and Experimental Pathology, AKH, University of Vienna, Vienna, A-1090, Austria Int. Arch. Allergy Immunol. (1997), 113(1-3), 260-261 CODEN: IAAIEG; ISSN: 1018-2438 Karger Journal English 15-9 (Immunochemistry) Patients allergic to tree pollen, fruit, and vegetables display IgE cross-reactivity to the major birch pollen allergen Bet v 1. In contrast to other major allergens, no continuous IgE epitopes have been identified for Bet v 1 as yet, indicating that the epitopes are of the conformational type. Previously, the authors produced an antibody, Bip 1, which was obsd. to enhance IgE binding to Bet v 1. Here, the authors expressed the Bip 1 Fab in Escherichia coli and characterized the purified recombinant Fab and its interaction with Bet v 1 by immunol. and spectroscopic methods. Bip 1 antibody birch allergen IgE

ST

IT

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AN

DN ТŢ

ΑU

CS

so.

PB

DT

LΑ

CC

AB

ST

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RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
        (Bet v I (Betula verrucosa, I); Bip 1 monoclonal antibody modulates
        human IgE binding to birch pollen group 1 allergen)
IT
     Birch (Betula pendula)
     Molecular association
        (Bip 1 monoclonal antibody modulates human IgE binding to birch pollen
        group 1 allergen)
IT
     IqE
     RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
        (Bip 1 monoclonal antibody modulates human IgE binding to birch pollen
        group 1 allergen)
TΨ
     Monoclonal antibodies
     RL: BAC (Biological activity or effector, except adverse); BIOL
     (Biological study)
        (Bip 1; modulation of human IgE binding to birch pollen group 1
        allergen by)
Ъ5
    ANSWER 11 OF 26 CAPLUS COPYRIGHT 2000 ACS
     1996:548557 CAPLUS
AN
DN
     125:193456
ΤT
     Immunoassay method and reagent involving suspendable carbon-labeled
    bioaffine particles
ΙN
     Loennberg, Maria; Carlsson, Jan
PΑ
     Pharmacia Ab, Swed.
SO
     PCT Int. Appl., 36 pp.
    CODEN: PIXXD2
DΤ
     Patent
LΑ
    English
IC
     ICM G01N033-543
     ICS G01N033-532
CC
     15-1 (Immunochemistry)
     Section cross-reference(s): 9, 14
FAN.CNT 1
                                        APPLICATION NO. DATE
     PATENT NO.
                    KIND DATE
                          -----
     ---- ----
                                         _____
PT
    WO 9622532
                     Α1
                           19960725
                                        WO 1996-SE42
                                                         19960118
        W: AU, CA, JP, US
        RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
                                    CA 1996-2210794 19960118
     CA 2210794
                 AA
                           19960725
    AU 9645928
                      A1
                           19960807
                                         AU 1996-45928
                                                          19960118
    EP 804733
                           19971105
                                         EP 1996-901591
                      A1
                                                           19960118
        R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE, IE
     JP 11505603
                     T2 19990521
                                         JP 1996-522207 19960118
PRAI SE 1995-184
                     19950120
    WO 1996-SE42
                     19960118
    An anal. method comprises establishing the presence of an analyte in a
     sample by forming a complex between the analyte and its bioaffine
     counterpart and a suspendable bioaffine reactant (R1) which is labeled
    with carbon particles and incorporated in the complex in an amt. related
    to the amt. of analyte in the sample. The method is characterized in
that
    a measurable part of the particles are able to settle. An immunoreagent
    is described that is labeled with particles and chosen from the group
IgE,
    anti-IgE antibody, or allergen, including IgE-reactive epitopes
    thereof, characterized in that the particles are carbon particles.
    immunoassay carbon particle bioaffinity label; allergen specific IgE detn
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TТ

Allergens

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carbon particle; immunochromatog carbon particle bioaffinity label; blood
     allergen IgE detn allergy diagnosis
ΙT
     Birch
     Mite and Tick
        (allergens; immunoassay method and reagent using suspendable
        carbon-labeled bioaffine particles)
TΤ
     Allergy
     Asthma
     Blood analysis
     Immunoassay
     Inflammation
     Polymer-supported reagents
        (immunoassay method and reagent using suspendable carbon-labeled
        bioaffine particles)
TΤ
     Antibodies
     RL: ANT (Analyte); ARG (Analytical reagent use); THU (Therapeutic use);
     ANST (Analytical study); BIOL (Biological study); USES (Uses)
        (immunoassay method and reagent using suspendable carbon-labeled
        bioaffine particles)
IΤ
     Allergens
     Antigens
     Caseins, biological studies
     RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL
     (Biological study); USES (Uses)
        (immunoassay method and reagent using suspendable carbon-labeled
        bioaffine particles)
IT
     Carbon black, uses
     RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
        (immunoassay method and reagent using suspendable carbon-labeled
        bioaffine particles)
TΥ
     Polyamide fibers, analysis
     RL: ARU (Analytical role, unclassified); DEV (Device component use); ANST
     (Analytical study); USES (Uses)
        (immunoassay method and reagent using suspendable carbon-labeled
        bioaffine particles)
ΙT
     Immunoglobulins
     RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL
     (Biological study); USES (Uses)
        (A, immunoassay method and reagent using suspendable carbon-labeled
        bioaffine particles)
IT
     Immunoglobulins
     RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL
     (Biological study); USES (Uses)
        (D, immunoassay method and reagent using suspendable carbon-labeled
        bioaffine particles)
TΤ
     Immunoglobulins
    RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL
     (Biological study); USES (Uses)
        (E, immunoassay method and reagent using suspendable carbon-labeled
        bioaffine particles)
IT
    Immunoglobulins
    RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL
     (Biological study); USES (Uses)
        (G, immunoassay method and reagent using suspendable carbon-labeled
       bioaffine particles)
    Immunoglobulins
    RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL
     (Biological study); USES (Uses)
```

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(M, immunoassay method and reagent using suspendable carbon-labeled
        bioaffine particles)
IT
     Immunoassay
        (immunoadsorption chromatog., immunoassay method and reagent using
        suspendable carbon-labeled bioaffine particles)
     9004-70-0, Nitrocellulose
TΤ
     RL: ARU (Analytical role, unclassified); DEV (Device component use); ANST
     (Analytical study); USES (Uses)
        (immunoassay method and reagent using suspendable carbon-labeled
        bioaffine particles)
ΙT
     7440-44-0, Carbon, uses
     RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
        (particles; immunoassay method and reagent using suspendable
        carbon-labeled bioaffine particles)
L5
     ANSWER 12 OF 26 CAPLUS COPYRIGHT 2000 ACS
     1997:474622 CAPLUS
ΑN
DN
     127:160510
     Diversity of human T cell receptor sequences of T cell clones with
TI
     specificity for Bet v 1 peptide/MHC II complexes
     Breiteneder, Heimo; Hajek, Roswitha; Huttinger, Robert; Ebner, Christof;
ΑU
     Schenk, Siegfried; Kraft, Dietrich; Scheiner, Otto
CS
     Institute of General and Experimental Pathology, AKH-EBO-3Q, University
of
     Vienna, Vienna, 1090, Austria
SO
     Adv. Exp. Med. Biol. (1996), 409 (New Horizons in Allergy Immunotherapy),
     365-374
     CODEN: AEMBAP; ISSN: 0065-2598
PB
     Plenum
DΤ
     Journal
LΑ
     English
CC
     15-9 (Immunochemistry)
AB
     T cell clones (TCC) were raised from the peripheral blood of patients
     suffering from tree pollen allergy. All TCC were restricted by HLA-DR
    mols. To investigate possible intervention targets in type I allergic
     diseases, the authors examd. T cell receptor (TCR) .alpha.- and
     .beta.-chain nucleotide sequences of several allergen-reactive human CD4+
     TCC specific for 4 frequently found epitopes of Bet v 1, the
    major birch pollen allergen. In general, TCC specific for the 4\,
     epitopes investigated, used diverse TCRAV and TCRBV gene segments.
    Moreover, the junctional regions encoding the third complementarity detg.
     regions (CDR3) of the TCR showed striking heterogeneities in length and
     amino acid compn. A more restricted use of two J gene segments (TCRBJ1S4
     and 2S7) was only obsd. in the .beta.-chain of TCR used by TCC specific
     for epitope 1. In addn., all TCC specific for epitope
     4 showed an arginine residue in the N-terminal region of their TCRBV CDR3
     loops despite their sequence diversities. In view of the striking
    heterogeneities found, therapeutic strategies aimed at the clonal
deletion
    of allergen-specific T cell clones, providing help for IgE synthesis, may
    not be feasible. Moreover, these results cast a doubt on the theory,
that
    the CDR3 exclusively provides the primary contact with the peptide bound
    in the major histocompatibility (MHC) groove, and suggest addnl.
    interaction with MHC class II.
    TCR usage T cell birch allergen
```

RL: BSU (Biological study, unclassified); BIOL (Biological study)

ΙT

Allergens

(Bet v I (Betula verrucosa, I); TCR receptor usage by HLA-DR-restricted human T cells specific for birch pollen allergen epitopes) TΤ CD4-positive T cell DNA sequences **Epitopes** Pollen Protein sequences (TCR receptor usage by HLA-DR-restricted human T cells specific for birch pollen allergen epitopes) HLA-DR antigen TCR .alpha..beta. (receptor) RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence) (TCR receptor usage by HLA-DR-restricted human T cells specific for birch pollen allergen epitopes) ΙT 150302-77-5 150302-78-6 167382-53-8 187540-70-1 RL: PRP (Properties) (TCR receptor usage by HLA-DR-restricted human T cells specific for birch pollen allergen epitopes) ANSWER 13 OF 26 CAPLUS COPYRIGHT 2000 ACS 1996:355269 CAPLUS ΑN DN 125:31847 TI Evidence for an alpha helical T cell epitope in the C-terminus of the main birch pollen allergen Bet v 1 ΑU Kungl, Andreas J.; Susani, Markus; Lindemann, Almut; Machius, Mischa; Visser, Antonie J. W. G.; Scheiner, Otto; Kraft, Dietrich; Breitenbach, Michael; Auer, Manfred CS Department Immunodermatology, Sandoz Research Institute, Vienna, A-1235, Austria SO Biochem. Biophys. Res. Commun. (1996), 223(1), 187-192 CODEN: BBRCA9; ISSN: 0006-291X DTJournal LA English CC 15-9 (Immunochemistry) Section cross-reference(s): 11 Secondary structure prediction of the main birch pollen allergen Bet  $v\ 1$ AB was in good agreement with the secondary structural elements found by analyzing the Bet v 1 CD data. According to both expt. and prediction, 32% of 160 amino acids participate in alpha helixes, 21% in beta sheets, 24% in turns, and 23% in other structural motifs. The peptide LRAVESYLLAHS which represents one of the major T cell epitopes on Bet v 1 was shown to have a high propensity to form an alpha helix. Time-resolved fluorescence anisotropy measurements of the allergen revealed an overall rotational correlation time of 7.35 ns, which corresponds to a hydrodynamic mol. radius of 19.2 .ANG.. This refers to monomeric Bet v 1 mol. in soln., which is also reflected in the narrow band width of the 1H-NMR spectrum. The results presented here are in good agreement with the recently solved NMR structure of Amb t 5; both allergens are monomers in soln. with an extended C-terminal alpha helix contg. a major T cell epitope. ST birch allergen Betv1 epitope alpha helix; T lymphocyte birch allergen Betv1 epitope ΙT Conformation and Conformers Pollen

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Protein sequences
        (alpha helical human T cell epitope in C-terminus of main
        birch pollen allergen Bet v 1)
IT
     Allergens
     RL: BOC (Biological occurrence); PRP (Properties); BIOL (Biological
     study); OCCU (Occurrence)
        (Bet v I (Betula verrucosa, I), alpha helical human T cell
      epitope in C-terminus of main birch pollen allergen Bet v 1)
ΙT
     Lymphocyte
        (T-cell, alpha helical human T cell epitope in C-terminus of
        main birch pollen allergen Bet v 1)
ΙT
     Conformation and Conformers
        (.alpha.-helical, alpha helical human T cell epitope in
        C-terminus of main birch pollen allergen Bet v 1)
ΙT
     151901-17-6
     RL: BOC (Biological occurrence); PRP (Properties); BIOL (Biological
     study); OCCU (Occurrence)
        (T-cell epitope; alpha helical human T cell epitope
        in C-terminus of main birch pollen allergen Bet v 1)
     ANSWER 14 OF 26 CAPLUS COPYRIGHT 2000 ACS
L5
     1996:546462 CAPLUS
ΑN
DN
     125:219490
TT
     High-level expression in Escherichia coli and purification of recombinant
     plant profilins: comparison of IgE-binding capacity and allergenic
     activity
ΑU
     Vrtala, Susanne; Wiedemann, Petra; Mittermann, Irene; Eichler,
Hans-Georg;
     Sperr, Wolfgang R.; Valent, Peter; Kraft, Dietrich; Valenta, Rudolf
     Inst. Generla Experimental Pathology, Univ. Vienna, Austria
     Biochem. Biophys. Res. Commun. (1996), 226(1), 42-50
SO
     CODEN: BBRCA9; ISSN: 0006-291X
DT
     Journal
LΑ
     English
CC
     15-9 (Immunochemistry)
     Because of their structural similarity and ubiquitous distribution as
     actin binding proteins, plant profilins represent important
cross-reactive
     allergens for almost 20% of patients suffering from Type I allergy to
     pollen and other plant products. The cDNAs coding for three birch
     profilin variants (Tyr44, Glu47, and Asn47), timothy grass profilin, and
     three tobacco profilin isoforms (ntprof1-3) were expressed at high levels
     in Escherichia coli as a non-fusion proteins. The recombinant plant
     profilins were purified to homogeneity by poly (L-proline) affinity
     chromatog. and showed comparable capacity to bind IgE-antibodies from
     profilin allergic patients. All recombinant plant profilins elicited
     dose-dependent histamine release from basophils of a profilin allergic
     patient and induced immediate type skin reactions. It is concluded that
     profilins from different plant species share IgE-epitopes and
     allergenic properties. Plant profilins therefore constitute a family of
     functional pan-allergens which may substitute each other for diagnosis
and
     specific immunotherapy.
ST
     profilin allergen IgE binding
ΙT
    Allergens
    RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
        (Bet v 2 (Betula verrucosa, 2); birch allergen
       binding by IgE from allergic humans)
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ΙT
     Basophil
        (IgE-binding capacity and allergenic activity of recombinant profilins
        from birch, timothy grass, and tobacco pollen in relation to histamine
        release by basophils)
ΙT
     Allergy
        (birch, timothy grass, and tobacco profilin binding by IgE from
        allergic humans)
TΤ
     Birch
     Escherichia coli
     Timothy
     Tobacco
        (high-level expression in Escherichia coli and comparison of
        IgE-binding capacity and allergenic activity of recombinant profilins
        from birch, timothy grass, and tobacco pollen)
ΤТ
     Profilins
     RL: BAC (Biological activity or effector, except adverse); BPR
(Biological
     process); BIOL (Biological study); PROC (Process)
        (high-level expression in Escherichia coli and comparison of
        IgE-binding capacity and allergenic activity of recombinant profilins
        from birch, timothy grass, and tobacco pollen)
IΤ
     Immunoglobulins
     RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
        (E, high-level expression in Escherichia coli and comparison of
        IgE-binding capacity and allergenic activity of recombinant profilins
        from birch, timothy grass, and tobacco pollen)
ΙT
     51-45-6, Histamine, biological studies
     RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
        (IgE-binding capacity and allergenic activity of recombinant profilins
        from birch, timothy grass, and tobacco pollen in relation to histamine
        release by basophils)
L5
     ANSWER 15 OF 26 CAPLUS COPYRIGHT 2000 ACS
AN
     1995:645495 CAPLUS
DN
     123:141599
TΙ
     Multiplicity of cross-reactive epitopes on Bet v I as detected
     with monoclonal antibodies and human IgE
     Akkerdaas, J. H.; van Ree, R.; Aalbers, M.; Stapel, S. O.; Aalberse, R.
ΑU
CS
     Central Laboratory, Netherlands Red Cross Blood Transfusion Service,
     Amsterdam, 1066 CX, Neth.
SO
     Allergy (Copenhagen) (1995), 50(3), 215-20
     CODEN: LLRGDY; ISSN: 0105-4538
DT
     Journal
     English
LA
CC
     15-9 (Immunochemistry)
     Section cross-reference(s): 17
     Six monoclonal antibodies against Bet v\ \mbox{I}, the major cross-reactive
AB
     allergen of birch pollen (Betula verrucosa), were obtained. Four did not
     react with fruits, but 2 monoclonal antibodies (mAbs) (5H8 and 9C11) were
     reactive with apple and other fruits. These 2 cross-reactive antibodies
     reacted with identical or overlapping sites, but differed in their
     relative degree of cross-reactivity toward various fruits and hazelnut.
     Cross-reactive human IgE antibodies reacted with a non-overlapping
     epitope, as indicated by results of a 2-site RIA with the
     fruit-reactive mAb 9C11. By isoelec. focusing (IEF) in conjunction with
     immunoblotting, a max. of 7 isoforms could be distinguished. Depletion
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```
birch-pollen ext. for Bet v I with the most reactive mAb (7F7) removed
     approx. 95% of the IgE cross-reactivity between birch pollen and apple
     ext. The remaining 5% cross-reactive material still could inhibit the
     binding of IgE to apple allergen completely, and was reactive with mAbs
     5H8 and 3C4. By IEF/immunoblot, it was shown that these mAbs recognize
an
     isoform of Bet v I that is poorly, if at all, recognized by mAb 7F7.
     These results illustrate the heterogeneity of Bet v I, both with respect
     to the cross-reactive sites as well as to the backbone structure. This
     type of heterogeneity has possible implications for the use of monoclonal
     antibodies in allergen standardization.
ST
     crossreactive epitope birch allergen
     antibody IgE
ΙT
     Alder
     Apple
     Birch
     Cherry
     Hazel
     Peach
     Pear
        (multiplicity of cross-reactive epitopes on birch
      allergen as detected with monoclonal antibodies and human IqE)
IΤ
     Allergens
     RL: PRP (Properties)
        (Bet v I (Betula verrucosa, I), multiplicity of cross-reactive
      epitopes on birch allergen as detected with
        monoclonal antibodies and human IgE)
ΙT
     Immunoglobulins
     RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
     (Uses)
        (E, multiplicity of cross-reactive epitopes on birch
      allergen as detected with monoclonal antibodies and human IgE)
ΙT
     Antibodies
     RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
        (monoclonal, multiplicity of cross-reactive epitopes on
      birch allergen as detected with monoclonal antibodies
        and human IgE)
     ANSWER 16 OF 26 CAPLUS COPYRIGHT 2000 ACS
ΑN
     1995:724208 CAPLUS
DN
     123:167018
     Diversity of TCRAV and TCRBV sequences used by human T-cell clones
     specific for a minimal epitope of Bet v 1, the major birch
     pollen allergen
AU
     Breiteneder, Heimo; Scheiner, Otto; Hajek, Roswitha; Hulla, Wolfgang;
     Huettinger, Robert; Fischer, Gottfried; Kraft, Dietrich; Ebner, Christof
CS
     Institute of General and Experimental Pathology, University of Vienna,
     Vienna, A-1090, Austria
SO
     Immunogenetics (1995), 42(1), 53-8
     CODEN: IMNGBK; ISSN: 0093-7711
DΤ
     Journal
     English
LΑ
CC
     15-2 (Immunochemistry)
     Section cross-reference(s): 3
AΒ
     T-cell clones (TCC) were raised from the peripheral blood of patients
     suffering from tree pollen allergy. All TCC were restricted by HLA-DR
     mols. To investigate possible intervention targets in Type I allergic
```

diseases, the authors examd. T-cell receptor (TCR) .alpha. and .beta. chain nucleotide sequences of five allergen-reactive human CD4+ TCC specific for a C-terminal epitope (BV 144) of Bet v 1, the major birch pollen allergen. Proliferation assays using synthetic peptides revealed the 10-mer LRAVESYLLA as minimal epitope for three TCC; two TCC also displayed reactivity with the nonapeptide LRAVESYLL. expressed TCRBV2S3, all other BV144-specific TCC used diverse TCRAV and TCRBV gene segments. Moreover, the junctional regions encoding the third complementary detg. regions (CDR3) of the TCR showed a striking heterogeneity in length and amino acid compn. Nevertheless, all TCC showed an arginine residue in the N-terminal region of their TCRBV CDR3 loops. Therefore, therapeutic strategies aimed at the clonal deletion of allergen-specific T-cell clones, providing help for IgE synthesis, will not be feasible. The results cast a doubt on the theory that the CDR3 exclusively provides the primary contact with the peptide bound in the major histocompatibility (MHC) groove, and suggest addnl. interaction with MHC class II. TCR alphabeta V region birch allergen; Betv1 allergen TCR alphabeta V region; gene TCRAV TCRBV diversity Betv1 allergen Gene, animal RL: PRP (Properties) (TCRAV11S1J6C; diversity of T-cell receptor TCRAV and TCRBV sequences used by human T-cell clones specific for minimal epitope of Bet v 1, major birch pollen allergen) Gene, animal RL: PRP (Properties) (TCRAV2S3J17S7C; diversity of T-cell receptor TCRAV and TCRBV sequences used by human T-cell clones specific for minimal epitope of Bet v 1, major birch pollen allergen) Gene, animal RL: PRP (Properties) (TCRAV5S1J21C; diversity of T-cell receptor TCRAV and TCRBV sequences used by human T-cell clones specific for minimal epitope of Bet v 1, major birch pollen allergen) Gene, animal RL: PRP (Properties)

(TCRAV8S1J9S5C; diversity of T-cell receptor TCRAV and TCRBV sequences used by human T-cell clones specific for minimal epitope of Bet v 1, major birch pollen allergen)

Gene, animal

TCC

ST

IT

TΤ

ΙT

IT

RL: PRP (Properties)

(TCRAV8S2J9S15C; diversity of T-cell receptor TCRAV and TCRBV sequences

> used by human T-cell clones specific for minimal epitope of Bet v 1, major birch pollen allergen)

ΙT Gene, animal

RL: PRP (Properties)

(TCRAV9S1J9S3C; diversity of T-cell receptor TCRAV and TCRBV sequences used by human T-cell clones specific for minimal epitope of Bet v 1, major birch pollen allergen)

TΤ Gene, animal

RL: PRP (Properties)

(TCRBV15S1D1J2S5C2; diversity of T-cell receptor TCRAV and TCRBV sequences used by human T-cell clones specific for minimal epitope of Bet v 1, major birch pollen allergen)

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IT
     Gene, animal
     RL: PRP (Properties)
        (TCRBV17S1D1J2S3C2; diversity of T-cell receptor TCRAV and TCRBV
        sequences used by human T-cell clones specific for minimal
      epitope of Bet v 1, major birch pollen allergen)
IT
     Gene, animal
     RL: PRP (Properties)
        (TCRBV24S1D1J2S2C2; diversity of T-cell receptor TCRAV and TCRBV
        sequences used by human T-cell clones specific for minimal
      epitope of Bet v 1, major birch pollen allergen)
IT
     Gene, animal
     RL: PRP (Properties)
        (TCRBV2S3D1J1S5C1; diversity of T-cell receptor TCRAV and TCRBV
        sequences used by human T-cell clones specific for minimal
      epitope of Bet v 1, major birch pollen allergen)
ΙT
     Gene, animal
     RL: PRP (Properties)
        (TCRBV2S3D2J2S1C2; diversity of T-cell receptor TCRAV and TCRBV
        sequences used by human T-cell clones specific for minimal
      epitope of Bet v 1, major birch pollen allergen)
IT
     Birch
        (B. pendula, diversity of T-cell receptor TCRAV and TCRBV sequences
        used by human T-cell clones specific for minimal epitope of
        Bet v 1, major birch pollen allergen)
TΤ
     Allergens
     RL: ADV (Adverse effect, including toxicity); BPR (Biological process);
     BIOL (Biological study); PROC (Process)
        (Bet v I (Betula verrucosa, I), diversity of T-cell receptor TCRAV and
        TCRBV sequences used by human T-cell clones specific for minimal
     epitope of Bet v 1, major birch pollen allergen)
ΙT
     Immunoglobulins
     RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
        (E, diversity of T-cell receptor TCRAV and TCRBV sequences used by
        human T-cell clones specific for minimal epitope of Bet v 1,
        major birch pollen allergen)
     Histocompatibility antigens
IT
     RL: ADV (Adverse effect, including toxicity); BPR (Biological process);
     BIOL (Biological study); PROC (Process)
        (HLA-DR, diversity of T-cell receptor TCRAV and TCRBV sequences used
by
        human T-cell clones specific for minimal epitope of Bet v 1,
        major birch pollen allergen)
ΙT
    Lymphocyte
        (T-cell, diversity of T-cell receptor TCRAV and TCRBV sequences used
by
        human T-cell clones specific for minimal epitope of Bet v 1,
        major birch pollen allergen)
IT
    Antigen receptors
    Receptors
    RL: PRP (Properties)
        (TCR (T-cell antigen receptor), diversity of T-cell receptor TCRAV and
        TCRBV sequences used by human T-cell clones specific for minimal
     epitope of Bet v 1, major birch pollen allergen)
IT
    Antigen receptors
    Receptors
    RL: ADV (Adverse effect, including toxicity); BOC (Biological
occurrence);
    BPR (Biological process); PRP (Properties); BIOL (Biological study); OCCU
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(Occurrence); PROC (Process)
         (TCR .alpha..beta. (T-cell antigen receptor .alpha..beta.), diversity
         of T-cell receptor TCRAV and TCRBV sequences used by human T-cell
         clones specific for minimal epitope of Bet v 1, major birch
         pollen allergen)
 TΨ
      Deoxyribonucleic acid sequences
         (complementary, diversity of T-cell receptor TCRAV and TCRBV sequences
         used by human T-cell clones specific for minimal epitope of
         Bet v 1, major birch pollen allergen)
 ΙT
      167382-53-8 167382-54-9
      RL: ADV (Adverse effect, including toxicity); BPR (Biological process);
      BIOL (Biological study); PROC (Process)
         (as epitope for T-cell; diversity of T-cell receptor TCRAV
         and TCRBV sequences used by human T-cell clones specific for minimal
       epitope of Bet v 1, major birch pollen allergen)
      164272-40-6, Genbank Z47366 164272-41-7, Genbank Z47367 164272-42-8,
      Genbank Z47368
                     164272-43-9, Genbank Z47369 164272-44-0, Genbank
 Z47371
      164272-45-1, Genbank Z47370 164272-46-2, Genbank Z47372
      Genbank Z47373 164272-48-4, Genbank Z47374 164272-49-5, Genbank
 247375
      164272-50-8, Genbank Z47376
      RL: PRP (Properties)
         (nucleotide sequence; diversity of T-cell receptor TCRAV and TCRBV
         sequences used by human T-cell clones specific for minimal
       epitope of Bet v 1, major birch pollen allergen)
      ANSWER 17 OF 26 CAPLUS COPYRIGHT 2000 ACS
 ΑN
      1994:506526 CAPLUS
 DN
      121:106526
      Peptides of the main allergens contained in the pollen of trees of the
 TI
      Fagales order for use in diagnosing or treating allergies
 ΤN
      Ebner, Christof; Ferreira, Fatima; Schenk, Siegfried; Szepfalusi, Zsolt;
      Valenta, Rudolf; Breitenbach, Michael; Kraft, Dietrich; Rumpold, Helmut;
      Scheiner, Otto
 PA
      Biomay Produktions- und Handelsgesellschaft m.b.H., Austria
 SO
      PCT Int. Appl., 11 pp.
      CODEN: PIXXD2
 DT
      Patent
 LΑ
      German
 IC
      ICM C07K007-08
      ICS A61K039-36; G01N033-68
 CC
      15-9 (Immunochemistry)
 FAN. LNT 1
      PATENT NO.
                     KIND DATE
                                         APPLICATION NO. DATE
      -----
                                          -----
                     A2
ΡI
     WO 9410194
                            19940511
                                          WO 1993-AT163 19931025
      WO 9410194
                      A3 19940901
         W: AU, CA, FI, JP, NO, US
         RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
     AU 9454115
                      A1
                            19940524 AU 1994-54115
                                                           19931025
 PRAI AT 1992-2125
                      19921027
      AT 1993-43
                      19930114
     WO 1993-AT163
                     19931025
      The invention concerns the Teell epitope of a 17 kD protein
      present as the main allergen contained in the pollen of trees of the
      Fagales order, in particular birches, hazels and alders, or generated by
      genetic engineering as a recombinant protein. Because of the high degree
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of affinity between said trees, their resp. 17 kD proteins are also highly homologous. These proteins are designed as Bet v I, Cor a I and Aln q I in the international literature and cause tree pollen allergies in predisposed persons (allergic patients). The peptides derived from the main allergens (major allergens), in particular Bet v I, are suitable for diagnosing tree pollen allergy and are capable of stimulating (causing the proliferation, the cytokine prodn.) or blocking T-cells of the patients in vitro and in vivo in an allergen-specific manner, or to provoke tolerance to the allergen specific T-cells. Peptides of Bet v I which stimulate Tcells from patients allergic to birch trees were identified. crossreactivity of T cells from patients allergic to hazels and alders with these peptides was significant. ST birch allergen Bet v I peptide; allergy diagnosis treatment birch allergen peptide ΙT Allergens RL: BIOL (Biological study) (Aln g I, peptides of, for diagnosis and treatment of allergies) IT Allergy (diagnosis of, peptides of primary allergen of Fagales trees for) IΤ Allergy inhibitors (peptides of primary allergen of Fagales trees as) ΙT (primary allergen Aln g I of, peptides of, for diagnosis and treatment of allergies) ΙT Birch (primary allergen Bet v I of, peptides of, for diagnosis and treatment of allergies) ΙT (primary allergen Cor a I of, peptides of, for diagnosis and treatment of allergies) ITFagales (primary allergen of, peptides of, for diagnosis and treatment of allergies) ΙT Allergens RL: BIOL (Biological study) (Bet v I (Betula verrucosa, I), peptides of, for diagnosis and treatment of allergies) Allergens IT RL: BIOL (Biological study) (Cor a I (Corylus avellana, I), peptides of, for diagnosis and treatment of allergies) IT 150302-72-0, Allergen Bet v I(1-16) (birch) 150302-73-1, Allergen Bet v I(35-48) (birch) 150302-74-2, Allergen Bet v I(75-90) (birch) 150302-79-7, Allergen Bet v I (111-126) (birch) 150321-14-5, Allergen Bet v I(29-44) (birch) 152647-59-1, Allergen Bet v I (141-159) (birch) 156880-97-6, Allergen Bet v I(9-26) (birch) 156880-98-7, Allergen Bet v I(61-76) (birch) 156880-99-8, Allergen Bet v I (84-97) (birch) 156881-00-4, Allergen Bet v I (93-110) (birch) RL: BIOL (Biological study) (T-cell epitope of Bet v I allergen, for allergy diagnosis and treatment) L5ANSWER 18 OF 26 CAPLUS COPYRIGHT 2000 ACS AN1993:595664 CAPLUS DN 119:195664

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TΙ
     Histamine derivatives and methods for their use as immunomodulators
IN
     Melmon, Kenneth L.; Greenstein, Julia L.; Khosropour, Parisa
     Immulogic Pharmaceutical Corp., USA; Leland Stanford Junior University
PA
SO
     PCT Int. Appl., 39 pp.
     CODEN: PIXXD2
DT
     Patent
LΑ
     English
     ICM A61K031-415
     ICS A61K039-35; A61K039-39
     1-7 (Pharmacology)
FAN.CNT 1
     PATENT NO.
                    KIND DATE
                                         APPLICATION NO. DATE
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                                          -----
PΙ
     WO 9314754
                      A1
                            19930805
                                          WO 1993-US659
                                                           19930125
         W: AU, CA, FI, JP, KP, KR, NO, NZ
         RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
     CN 1079908
                                          CN 1993-102513 19930122
                     Α
                           19931229
     AU 9335915
                                          AU 1993-35915
                      A1
                            19930901
                                                           19930125
     EP 626847
                           19941207
                      A1
                                          EP 1993-904613
                                                          19930125
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT,
SE
     JP 07503470
                       Т2
                            19950413
                                          JP 1993-513377
                                                           19930125
PRAI US 1992-826180
                      19920127
     WO 1993-US659
                      19930125
     Methods are provided for using histamine derivs. His-NH(CH2)nCONHC6H4CF3
     (n = 2-10) as immunomodulators and in immunotherapeutics. More
     specifically, methods are provided for inhibiting at least a portion of
an
     antigen-specific antibody response and/or a portion of a T-cell
     proliferative response by the immune system of a mammal, comprising
     administering to the mammal an effective amt. of a compn. comprising
     .gtoreq.1 histamine deriv. having binding specificity for .gtoreq.1
     histamine receptor. Also disclosed are methods for treating sensitivity
     to a particular antigen and methods of treated T-cell-mediated disease in
     a person by administering a therapeutically effective amt. of a compn.
     comprising .gtoreq.1 histamine deriv. having binding specificity for
     .gtoreq.1 histamine receptor, optionally administering the antigen or an
     immunogenic portion thereof, and further optionally administering a
     peptide comprising .gtoreq.1 T-cell epitope of the antigen.
     Examples showed that histamine congeners are potent immunosuppressants,
     and that each has a different potential mechanism of immunomodulation.
     His-NHCH(CH3)(CH2)4CONHC6H4CF3 suppresses T-cell-dependent IgE and IgG1
     (but not IgM, IgG2a, or IgG2b) antibody responses. His-
    NH(CH2)5CONHC6H4CF3 (I) suppresses IgG1, IgG2a, and IgG2b (but not IgM)
     responses. Only I appears to directly suppress T-cell proliferation to
     specific antigen at the doses tested. Effects of the derivs. in an
     autoimmune disease model are presented.
    immunosuppressant histamine deriv
ST
ΙT
     Antigens
    RL: BIOL (Biological study)
        (T-cell antigen-specific proliferative response inhibition by
histamine
       deriv. and)
IΤ
    Alder
    Alternaria
    Artemisia
    Birch
    Blattella
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Canidae
     Cryptomeria
     Dermatophagoides
     Felis
     Honeybee
     Lolium
     Oak
     Olea
     Parietaria
     Periplaneta
     Plantago
     Ragweed
        (allergen protein of, sensitivity to, treatment of, histamine
        derivs. for)
IT
     Poisoning
        (endotoxin-induced, treatment of, immunosuppressant histamine derivs.
        for)
ΙT
     Allergy inhibitors
     Immunosuppressants
        (histamine derivs.)
TТ
     Antidiabetics and Hypoglycemics
        (immunosuppressant histamine derivs.)
ΙT
     Peptides, biological studies
     RL: BIOL (Biological study)
        (of allergen T-cell epitope, histamine deriv. and, for
        inhibition of allergen-specific antibody response)
IT
     Transplant and Transplantation
        (rejection of, treatment of, immunosuppressant histamine derivs. for)
ΙT
     Lymphocyte
        (T-cell, antigen-specific proliferative response of, inhibition of,
        histamine derivs. for)
IΤ
     Neoplasm inhibitors
        (T-cell leukemia, immunosuppressant histamine derivs.)
ΙT
     Antigens
     RL: BIOL (Biological study)
        (auto-, sensitivity to, treatment of, histamine derivs. for)
IT
     Allergy inhibitors
        (desensitizers, histamine derivs.)
IT
     Toxins
     RL: BIOL (Biological study)
        (endo-, poisoning induced by, treatment of, immunosuppressant
histamine
        derivs. for)
IT
     Receptors
     RL: BIOL (Biological study)
        (histaminic, histamine derivs. binding to, for immunosuppressants)
IT
     Therapeutics
        (immuno-, histamine derivs., for T-cell mediated diseases)
IT
     Skin, neoplasm
        (mycosis fungoides, treatment of, immunosuppressant histamine derivs.
        for)
IT
     150436-86-5
                   150643-50-8
                                  150643-51-9
                                                150643-52-0
                                                              150643-59-7
     150643-60-0
                   150643-61-1
                                  150643-62-2
                                                150643-63-3
     RL: BIOL (Biological study)
        (as immunosuppressant)
IT
     51-45-6D, Histamine, derivs.
     RL: BIOL (Biological study)
        (as immunosuppressants)
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IT
     150436-88-7
     RL: BIOL (Biological study)
        (histamine receptor binding by and immunosuppressant activity of)
IT
     150436-87-6
     RL: BIOL (Biological study)
        (histamine receptor binding by, immunosuppressant histamine derivs. in
        relation to)
    ANSWER 19 OF 26 CAPLUS COPYRIGHT 2000 ACS
Ъ5
    1993:493527 CAPLUS
ΑN
DN
    119:93527
TΙ
     Recombitope peptides containing T cell epitopes and stimulating
     T cell activity, for allergy therapy and diagnosis
     Rogers, Bruce L.; Morgenstern, Jay P.; Bond, Julian F.; Garman, Richard
    D.; Kuo, Mei Chang; Morville, Malcolm
PΑ
     Immulogic Pharmaceutical Corp., USA
SO
    PCT Int. Appl., 73 pp.
    CODEN: PIXXD2
DT
    Patent
LΑ
    English
    ICM C12N015-12
IC
    ICS A61K039-35; C12N015-62; G01N033-53; C07K007-10; C07K015-08;
         A61K039-36
CC
    15-9 (Immunochemistry)
FAN.CNT 7
    PATENT NO.
                    KIND DATE
                                         APPLICATION NO. DATE
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PΙ
    WO 9308280
                     A1
                           19930429
                                         WO 1992-US8694 19921016
        W: AU, CA, FI, HU, JP, KR, NO
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE
    US 5547669
                           19960820
                     A
                                       US 1991-807529
                                                          19911213
    ZA 9208000
                     Α
                           19930426
                                         ZA 1992-8000
                                                          19921016
    AU 9227940
                     A1
                           19930521
                                        AU 1992-27940
                                                          19921016
    AU 682658
                     B2
                           19971016
    ZA 9208001
                    A
                           19930622
                                         ZA 1992-8001
                                                          19921016
    EP 610335
                     A1
                          19940817
                                         EP 1992-922494 19921016
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE
    JP 07503362
                    Т2
                           19950413
                                        JP 1992-507748 19921016
    WO 9424281
                     A1
                           19941027
                                         WO 1993-US3471
                                                          19930414
        W: AU, CA, FI, JP, KR, NO, NZ, UA
        RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
    AU 9341026
                     A1
                           19941108
                                         AU 1993-41026
                                                         19930414
    AU 680820
                      В2
                           19970814
    EP 694067
                     A1
                           19960131
                                         EP 1993-910592
                                                          19930414
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT,
SE
    JP 09501043
                      Т2
                           19970204
                                         JP 1993-523074
                                                          19930414
                     Α
    NO 9401370
                           19940608
                                         NO 1994-1370
    FI 9401758
                     Α
                           19940616
                                        FI 1994-1758
                                                          19940415
    FI 9504895
                     Α
                           19951013
                                        FI 1995-4895
                                                          19951013
    NO 9504095
                     A
                           19951213
                                        NO 1995-4095
                                                          19951013
    FI 9603331
                     Α
                           19960827
                                        FI 1996-3331
                                                         19960827
PRAI US 1991-777859 19911016
    US 1991-807529 19911213
    US 1989-431565
                     19891103
    US 1991-662276
                     19910228
    WO 1992-US8694
                     19921016
    WO 1993-US3471 19930414
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FT 1995-4895
                      19951013
     Recombitope peptides, stimulating T cell activity and comprising
.gtoreq.2
     T cell epitopes derived from the same or from different protein
     antigens, are provided. The peptides can be derived from protein
     allergens, autoantigens, or other protein antigens. Methods of
diagnosing
     sensitivity to an allergen or other protein antigen, methods to treat
such
     sensitivity, methods for designing recombitope peptides where the protein
     antigen has unknown or ill-defined T cell epitopes, and
     therapeutic compns. are also disclosed. T cell epitopic studies were
     with peptides and protein chains of the human T cell-reactive feline
     protein (TRFP) and immunoreactive regions were identified. Synthetic
     oligonucleotides were designed with Escherichia coli-preferred codons for
     PCR amplification and expression in E. coli of recombitope peptides from
     TRFP. The peptide sequences included a 6 His residue leader sequence
(for
     allowing purifn. of the expressed recombitope peptide using QIAGEN
     NTA-agarose) and a thrombin cleavage site before the actual recombitope
     sequence. Recombitope peptide arrangements were identified which had
     little to no binding to IgE and which gave responses to T cells of
     patients allergic to TRFP.
ST
     recombitope peptide T lymphocyte stimulation epitope; allergen
     recombitope peptide T cell stimulation; autoantigen recombitope peptide T
     cell stimulation; antigen recombitope peptide T cell stimulation; allergy
     diagnosis treatment recombitope peptide; cat allergy recombitope peptide;
     T cell reactive feline protein recombitope
ΙT
     Allergens
     RL: BIOL (Biological study)
        (T cell epitopes of, in recombitope peptides stimulating T
        cells)
TΤ
     Allergy inhibitors
        (T cell epitopes-contg. T cell-stimulating recombitope
        peptides as)
ΙT
    Allergy
        (T cell epitopes-contg. T cell-stimulating recombitope
        peptides for detection and modification of)
ΙT
     Antigens
     RL: BIOL (Biological study)
        (T cell epitopes-contg. T cell-stimulating recombitope
       peptides from, designing of)
ΙT
     Proteins, specific or class
     RL: BIOL (Biological study)
        (TRFP (human T cell-reactive feline protein), T cell epitopes
       of, T cell-stimulating recombitope peptides contg.)
ΙT
    Alder
    Alternaria
    Artemisia
    Birch
    Blattella
    Canidae
    Cryptomeria
    Dermatophagoides
    Dermatophagoides farinae
    Dermatophagoides pteronyssinus
    Felidae
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Honeybee
     Lolium
     0ak
     Olea
     Parietaria
     Periplaneta
     Plantago
     Ragweed
        (allergen of, T cell epitopes of, in recombitope
        peptides stimulating T cells)
IΤ
     Blood analysis
        (detection of T cells and Igs to protein antiqen in, recombitope
        peptides contg. T cell epitopes and T cell-stimulating
        activity for)
ΙT
     Immunoglobulins
     RL: BIOL (Biological study)
        (detection of T cells and, to protein antigen, recombitope peptides
        contg. T cell epitopes and T cell-stimulating activity for)
IT
     Nucleic acids
     RL: BIOL (Biological study)
        (for T cell epitopes-contg. T cell-stimulating recombitope
        peptides)
ΙT
     Protein sequences
        (of T cell-stimulating recombitope peptides of human T cell-reactive
        feline protein of cat)
     Proteins, biological studies
IT
     RL: BIOL (Biological study)
        (of basement membrane, as autoantiques, T cell epitopes
        -contg. T cell-stimulating recombitope peptides from)
ΙT
     Receptors
     RL: BIOL (Biological study)
        (of thyroid cells, as autoantigen, T cell epitopes-contq. T
        cell-stimulating recombitope peptides from)
IΤ
     Basement membrane
        (proteins of, as autoantigen, T cell epitopes-contg. T
        cell-stimulating recombitope peptides from)
ΙT
     Thyroid gland, composition
        (proteins or receptors of, as autoantigens, T cell epitopes
        -contg. T cell-stimulating recombitope peptides from)
ΙT
     Peptides, biological studies
     RL: BIOL (Biological study)
        (recombitopes, T cell epitopes on and T cell stimulating)
IT
     Felis catus
        (sensitivity to, treatment of, T cell epitopes-contg. T
        cell-stimulating recombitope peptides for)
IT
     Multiple sclerosis
        (treatment of, with T cell epitopes-contg. T cell-stimulating
        recombitope peptides from myelin basic protein of human)
IT
     Allergens
     RL: BIOL (Biological study)
        (Lol p I (Lolium perenne, I), recombitope peptide contq. region of,
for
        T cell stimulation)
IT
    Allergens
     RL: BIOL (Biological study)
        (Lol p IX (Lolium perenne, IX), recombitope peptide contq. region of,
        for T cell stimulation)
TT
    Allergens
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RL: BIOL (Biological study)
        (Amb a I.4 (Ambrosia artemisifolia, I.4), recombitope peptide contg.
        region of, for T cell stimulation)
ΙT
     Allergens
     RL: BIOL (Biological study)
        (Amb a II (Ambrosia artemisifolia, II), recombitope peptide contg.
        region of, for T cell stimulation)
ΙT
     Immunoglobulins
     RL: BIOL (Biological study)
        (E, T cell-stimulating recombitope peptides contg. T cell
      epitopes not stimulating)
ΙT
     Phospholipoproteins
     RL: BIOL (Biological study)
        (MBP (myelin basic protein), as autoantigen, T cell epitopes
        -contq. T cell-stimulating recombitope peptides from)
IT
     Blood-group substances
     RL: BIOL (Biological study)
        (Rh, as autoantigen, T cell epitopes-contg. T
        cell-stimulating recombitope peptides from)
IΤ
     Lymphocyte
        (T-cell, recombitope peptides with epitopes for and
        stimulating)
IT
     Antigens
     RL: BIOL (Biological study)
        (auto-, T cell epitopes-contg. T cell-stimulating recombitope
        peptides from)
IT
     Receptors
     RL: BIOL (Biological study)
        (cholinergic, as autoantigen, T cell epitopes-contq. T
        cell-stimulating recombitope peptides from)
ΙT
     Deoxyribonucleic acid sequences
        (complementary, for human T cell-reactive feline protein of cat,
        recombitope peptides prepn. in relation to)
    Allergy
IT
        (delayed hypersensitivity, detection of, T cell epitopes
        -contg. T cell-stimulating recombitope peptides for)
ΙT
    Allergy
        (immediate hypersensitivity, detection of, T cell epitopes
        -contg. T cell-stimulating recombitope peptides for)
IT
    Allergens
     RL: BIOL (Biological study)
        (Der f I (Dermatophagoides farinae, I), recombitope peptide contg.
        region of, for T cell stimulation)
ΙT
    Allergens
    RL: BIOL (Biological study)
        (Der f II (Dermatophagoides farinae, II), recombitope peptide contg.
        region of, for T cell stimulation)
ΙT
    Allergens
    RL: BIOL (Biological study)
        (Der p I (Dermatophagoides pteronyssinus, I), recombitope peptide
        contg. region of, for T cell stimulation)
IΤ
    Allergens
    RL: BIOL (Biological study)
        (Der p II (Dermatophagoides pteronyssinus, II), recombitope peptide
        contg. region of, for T cell stimulation)
IT
    Allergens
    RL: BIOL (Biological study)
        (Amb a I (Ambrosia artemisifolia, I), recombitope peptide contg.
region
                                                                        Page 37
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of, for T cell stimulation)
     Allergens
ΤТ
     RL: BIOL (Biological study)
         (Amb a I.1 (Ambrosia artemisifolia, I.1), recombitope peptide contq.
        region of, for T cell stimulation)
IT
     Allergens
     RL: BIOL (Biological study)
        (Amb a I.2 (Ambrosia artemisifolia, I.2), recombitope peptide contg.
        region of, for T cell stimulation)
IT
     Allergens
     RL: BIOL (Biological study)
        (Amb a I.3 (Ambrosia artemisifolia, I.3), recombitope peptide contg.
        region of, for T cell stimulation)
ΙT
     Allergens
     RL: BIOL (Biological study)
        (Cry j I (Cryptomeria japonica, I), recombitope peptide contg. region
        of, for T cell stimulation)
IT
     Allergens
     RL: BIOL (Biological study)
        (Cry j II, recombitope peptide contg. region of, for T cell
        stimulation)
     136796-96-8, Leader A-human T cell-reactive feline protein chain 1 (cat)
IΤ
     136796-97-9, Leader B-human T cell-reactive feline protein chain 1 (cat)
     144996-55-4, Human T cell-reactive feline protein chain 2 (cat)
     RL: BIOL (Biological study)
        (amino acid sequence of and T cell epitopes-contg. T
        cell-stimulating recombitope peptides recombinant prepn. in relation
ΙT
     9004-10-8, Insulin, biological studies 9024-58-2
                                                          81876-95-1.
     Carboxypeptidase H
     RL: BIOL (Biological study)
        (as autoantigen, T cell epitopes-contg. T cell-stimulating
        recombitope peptides from)
ΙT
     149013-73-0
     RL: BIOL (Biological study)
        (as leader sequence in purifn. and prepn. of recombitope peptide from
        human T cell-reactive feline protein)
IT
     149119-96-0
                   149119-97-1
                                 149120-00-3
     RL: BIOL (Biological study)
        (nucleotide sequence of and T cell epitopes-contg. T
        cell-stimulating recombitope peptides recombinant prepn. in relation
IT
     136380-69-3, Human T cell-reactive feline protein chain 1 (29-55) (cat
     synthetic)
                  136380-84-2, Human T cell-reactive feline protein chain 2
     (14-39) (cat synthetic)
                               136380-92-2, Human T cell-reactive feline
     protein chain 1 Fel-29 fragments (cat synthetic)
                                                        149013-72-9
     149230-58-0, Human T cell-reactive feline protein chain 1 (7-33) (cat
                  149230-59-1, Human T cell-reactive feline protein chain 1
     synthetic)
     fragments (cat synthetic)
     RL: BIOL (Biological study)
        (recombitope peptide contg., cat allergy detection and treatment with)
ΙT
     9002-04-4, Thrombin
     RL: BIOL (Biological study)
        (synthetic leader sequence cleavage with, in prepn. of recombitope
        peptide from human T cell-reactive feline protein)
L5
    ANSWER 20 OF 26 CAPLUS COPYRIGHT 2000 ACS
```

ΑN

1994:29263 CAPLUS

120:29263 DN ΤI T cell clones specific for Bet v I, the major birch pollen allergen, crossreact with the major allergens of hazel, Cor a I, and alder, Aln g I Ebner, Christof; Ferreira, Fatima; Hoffmann, Karin; Hirschwehr, Reinhold; ΑU Schenk, Siegfried; Szepfalusi, Zsolt; Breiteneder, Heimo; Parronchi, Paola; Romagnani, Sergio; et al. CS Inst. Gen. Exp. Pathol., Univ. Vienna, Austria SO Mol. Immunol. (1993), 30(15), 1323-9 CODEN: MOIMD5; ISSN: 0161-5890 DTJournal English LA CC 15-9 (Immunochemistry) Tree pollens are responsible for type I allergies during the flowering AB season in spring. Pollens from birch, hazel and alder constitute the most important allergen sources in this respect in the northern hemisphere. Human IgE antibodies, specific for the major allergens of these pollens, are known to crossreact, and in general every tree pollen allergic patient is sensitized to these three pollen allergens. In this study the authors investigated 8 T-helper cell clones (CD3+, CD4+, TCR.alpha./.beta.) with specificity for Bet v I, the major birch pollen allergen, as proved by reactivity with purified natural as well as with recombinant allergen. The T cell clones were used to investigate common T cell epitopes of the Bet v I mol. with Cor a I, the major allergen of hazel pollen and Aln g I, the major allergen of alder pollen. All 8 T cell clones reacted with all three proteins with different intensity. Moreover, three T cell clones, which were known to react with immunodominant T cell epitopes on the Bet v I mol., were tested for reactivity with dodecapeptides synthesized according to the corresponding homologous regions of the Cor a I and Aln g I sequence. All the peptides induced strong T cell proliferation, indicating the existence of multiple cross-reacting epitopes. These findings will have an impact on the prodn. of vaccines for immunotherapy of tree pollen allergies. ST Betula allergen T cell crossreactivity; birch allergen T cell crossreactivity hazel; alder T cell crossreactivity birch allergen; tree pollen allergen T cell crossreactivity IT Allergens RL: BIOL (Biological study) (Aln g I (Alnus glutinosa, I), T-cells to birch allergen crossreactivity with, in humans with type I allergy) IΤ Pollen (allergen I of, of birch, human allergic T-cells to, alder and hazel major allergen crossreactivity with) IT (major allergen I of, human allergic T-cells to, alder and hazel major allergen crossreactivity by) IT Alder Hazel (major allergen of, human allergic T-cells to birch major allergen crossreactivity with) IT Allergens RL: BIOL (Biological study) (Bet v I (Betula verrucosa, I), T-cells of humans with type I allergy to, alder and hazel major allergen crossreactivity with) IT Allergens RL: BIOL (Biological study) (Cor a I (Corylus avellana, I), T-cells to birch

```
allergen crossreactivity with, in humans with type I allergy)
IT
     Lymphocyte
        (T-cell, to major allergen I of birch, of humans with type I allergy,
        alder and hazel major allergen crossreactivity by)
TТ
     Allergy
        (immediate hypersensitivity, T-cells to birch major allergen I in
        humans with, alder and hazel major allergen crossreactivity with)
ΙT
     151901-22-3
                 151901-23-4
                                 151901-24-5
     RL: BIOL (Biological study)
        (of major allergen I of alder, human T-cells to birch major allergen
        crossreactivity with)
IT
     146819-50-3
                   151901-17-6
                                 151901-18-7
     RL: BIOL (Biological study)
        (of major allergen I of birch, human allergic T-cells to, alder and
        hazel major allergen crossreactivity with)
IT
     151901-19-8
                 151901-20-1
                                 151901-21-2
     RL: BIOL (Biological study)
        (of major allergen I of hazel, human T-cells to birch major allergen
        crossreactivity with)
     ANSWER 21 OF 26 CAPLUS COPYRIGHT 2000 ACS
L5
ΑN
     1993/167322
                 CAPLUS
DN
     118:167322
     Mentification of multiple T cell epitopes on Bet v I, the major
TΙ
     birch pollen allergen, using specific T cell clones and overlapping
     peptides
     Ebner, C.; Szepfalusi, Z.; Ferreira, F.; Jilek, A.; Valenta, R.;
Αy
     Parronchi, P.; Maggi, E.; Romagnani, S.; Scheiner, O.; Kraft, D.
CS
     Inst. Gen. Exp. Pathol., Univ. Vienna, Vienna, A-1090, Austria
SO
     J. Immunol. (1993), 150(3), 1047-54
     CODEN: JOIMA3; ISSN: 0022-1767
DT
     Journal
LA
     English
CC
     15-9 (Immunochemistry)
     Eleven T cell clones (TCC) with specificity for Bet v I were established
AΒ
     from the peripheral blood of six birch pollen allergic donors. Bet v\ I
is
     the major allergen of birch (Betula verrucosa) pollen and shows high
     homol. to the major allergens of pollens of other trees within the order
     Fagales (hazel, alder, hornbeam, oak, etc.), which represent important
     inhalant allergens in the northern hemisphere. The TCC were shown to
     react with purified natural, as well as with purified recombinant Bet v
I.
    All clones showed the helper cell phenotype (CD3+CD4+) and expressed the
    TCR-.alpha./.beta.. The cytokine prodn. pattern in response to
    stimulation with allergen resulted in enhanced prodn. of interleukin
     (IL)-4 in 9 of 11 clones. The clones were used for T cell epitope
    mapping on the Bet v I mol. For this purpose, peptides with a length of
     12 amino acids each and overlapping for 10 residues were synthesized
     following the amino acid sequence of Bet v I. These 75 peptides were
used
    to stimulate Bet v I-specific T cell clones. The expts. revealed 7
    distinct T cell epitopes on the Bet v I mol. The
    epitopes were scattered over the whole mol., 2 sequences were in
    agreement with an algorithm previously described for the prediction of T
    cell epitopes. In 3 cases, one could identify distinct TCC
    specificities within single individuals. Furthermore, for each donor,
    none of the peptides representing epitopes for TCC inhibited the
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binding of IgE antibodies to Bet v I. These results suggest that T cells
     and IgE antibodies from the same individual recognize different
structures
     on the Bet v I allergen.
     T cell epitope birch allergen; Betula
     allergen T cell epitope
IT
     Pollen.
        (of birch, Bet v I allergen of, T cell epitopes of)
IT
     Immunoglobulins
     RL: BIOL (Biological study)
        (E, binding epitopes for human, of Bet v I allergen)
ΙT
     Lymphocyte
        (T-cell, helper cell, allergen Bet v I multiple epitopes for)
IT
     Lymphokines and Cytokines
     RL: FORM (Formation, nonpreparative)
        (interleukin 4, formation of, by T cells, Bet v I allergen induction
        of)
IT
     Allergens
     RL: BIOL (Biological study)
        (Bet v I (Betula verrucosa, I), multiple epitopes of, for T
        cell, IgE binding epitopes different from)
IT
     146819-47-8
                   146819-48-9
                                 146819-49-0
                                               146819-50-3
                                                              146819-51-4
     146819-52-5
                   146819-53-6
                                 146819-54-7
     RL: BIOL (Biological study)
        (of Bet v I allergen, as T cell epitope)
L5
     ANSWER 22 OF 26 CAPLUS COPYRIGHT 2000 ACS
ΑN
     1994:52558 CAPLUS
DN
     120:52558
     Studies on the biological activities of the amino terminal epitope
TΙ
     23-38 from the major birch pollen allergen Bet v I
     Vik, H.; Steinsvaag, S. K.; Dybendal, T.; Florvaag, E.; Holen, E.;
ΑU
     Elsayed, S.
     Lab. Clin. Biochem., Univ. Bergen, Norway
   _Mol. Biol. Immunol. Allergens (1993), 223-5. Editor(s): Kraft, Dietrich;
     Sehon, Alec H. Publisher: CRC, Boca Raton, Fla.
     CODEN: 59QMA6
ĎΤ
     Conference
LA
     English
     15-9 (Immunochemistry)
CC
     Peptide Bet v I 23-38 was demonstrated to bind IgE in vitro by RAST
     inhibition, in vivo by pos. skin prick tests in birch allergic
     individuals, mast cell degranulation in nasal mucosa, and by binding
    birch-specific IgE in Prausnitz Kustner inhibition tests. Bet v I 23-38
     could be an IgE-binding haptenic epitope.
ST
    birch pollen allergen
ΙT
    Birch
        (allergen of pollen of, biol. activities of N-terminal
        fragment of)
TΨ
    Pollen
        (allergen of, of birch, biol. activities of N-terminal fragment of)
ΙT
    Allergens
    RL: BIOL (Biological study)
        (Bet v I (Betula verrucosa, I), biol. activities of N-terminal
fragment
    ANSWER 23 OF 26 CAPLUS COPYRIGHT 2000 ACS
```

L5

```
117:105712
ΤI
     Tree pollen allergens, cDNA encoding them, and their use in treatment and
     diagnosis of allergies
     Breiteneder, Heimo; Reikerstorfer, Arnold; Valenta, Rudolf;
TN
     Hoffmann-Sommergruber, Karin; Breitenbach, Michael; Kraft, Dietrich;
     Rumpold, Helmut; Scheiner, Otto; Ebner, Christof; Ferreira, Fatima
     Biomay Biotechnik Produktions- und Handelsgesellschaft m.b.H., Austria
PA
SO
     PCT Int. Appl., 56 pp.
     CODEN: PIXXD2
DT
     Patent
LΑ
     English
TC
     ICM C12N015-29
         C07K013-00; C12N015-70; G01N033-53; C12Q001-02; A61K037-02
CC
     3-2 (Biochemical Genetics)
     Section cross-reference(s): 9, 15
FAN.CNT 1
     PATENT NO.
                     KIND DATE
                                          APPLICATION NO. DATE
     ______
                     ____
ΡI
     WO 9202621
                      A2
                            19920220
                                          WO 1991-EP1479
                                                           19910806
     WO 9202621
                      A3
                            19920514
        W: AU, CA, FI, JP, NO, US
         RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE
     AT 9001668
                      Α
                           19951115
                                          AT 1990-1668
                                                           19900808
     AT 401179
                      В
                            19960725
     CA 2067144
                      AΑ
                                          CA 1991-2067144 19910806
                            19920209
     AU 9183112
                      A1
                            19920302
                                          AU 1991-83112
                                                           19910806
     AU 657917
                      В2
                            19950330
     EP 495052
                      A1
                           19920722
                                          EP 1991-914150
                                                           19910806
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE
     JP 05501656
                    Т2
                           19930402
                                          JP 1991-513157
                                                           19910806
     FI 9201524
                      Α
                           19920407
                                          FI 1992-1524
                                                          19920407
     NO 9201362
                      Α
                           19920605
                                          NO 1992-1362
                                                           19920407
     US 5693495
                      Α
                           19971202
                                          US 1992-847010
                                                           19920601
    AU 9513436
                      A1
                           19950629
                                          AU 1995-13436
                                                           19950222
PRAI AT 1990-1668
                     19900808
     US 1991-683831
                      19910411
     WO 1991-EP1479
                     19910806
     CDNAs encoding alder pollen allergen Aln g I, hazel pollen allergen Cor a
AΒ
     I, and birch pollen allergen Bet v I are cloned and expressed in
     Escherichia coli. The allergens were recognized by IgE antibodies from
     sera of patients allergic to these pollens.
ST
     tree pollen allergen cDNA cloning; Aln g I allergen cDNA cloning; Cor a I
     allergen cDNA cloning; Bet v I allergen cDNA cloning; allergy treatment
    diagnosis pollen cDNA
IT
     Gene, plant
    RL: BIOL (Biological study)
        (CDNA, for pollen allergens Aln g I and Cor a I and Bet v I of alder
        and hazel and birch, cloning and expression in Escherichia coli of)
ΙT
    Molecular cloning
        (of cDNAs for pollen allergens Aln g I and Cor a I and Bet v I of
alder
       and hazel and birch, in Escherichia coli)
    Deoxyribonucleic acid sequences
IT
        (of Aln g I and Cor a I and Bet v I pollen allergen cDNAs of alder and
       hazel and birch)
ΙT
    Protein sequences
        (of Aln g I and Cor a I and Bet v I pollen allergen of alder and hazel
```

Page 42

ΑN

DN

1992:505712 CAPLUS

and birch) ΤТ Birch (pollen allergen Bet v I of, cDNA for, cloning and expression in Escherichia coli of) ΤТ Alder (pollen allergen Aln g I of, cDNA for, cloning and expression in Escherichia coli of) IT Hazel (pollen allergen Cor a I of, cDNA for, cloning and expression in Escherichia coli of) ΙT Fagales (pollen allergens of, cDNAs for, cloning and expression in Escherichia coli of) IT Allergy (treatment and diagnosis of, pollen allergens of hazel and birch and alder for) ΤТ Allergens RL: BIOL (Biological study) (Aln g I, cDNA for, of Aldus, cloning and expression in Escherichia IT Allergens RL: BIOL (Biological study) (Cor a I, cDNA for, of Corylus, cloning and expression in Escherichia coli of) ΙT Immunoglobulins RL: ANT (Analyte); ANST (Analytical study) (E, detection of, in allergy patients, pollen allergens of hazel and birch and alder for) ΙT Allergens RL: BIOL (Biological study) (Bet v I (Betula verrucosa, I), cDNA for, of Betula, cloning and expression in Escherichia coli of) ΙT 126161-14-6, Allergen Bet v I (Betula pendula clone pBV1 isoform protein 143066-16-4, Allergen Aln g I (alder) moiety) 143066-17-5, Allergen Cor a I (hazel isoform 1) 143066-18-6, Allergen Cor a I (hazel isoform 143066-19-7, Allergen Cor a I (hazel isoform 3) 143066-20-0, Allergen Cor a I (hazel isoform 4) RL: BAC (Biological activity or effector, except adverse); PRP (Properties); BIOL (Biological study) (amino acid sequence of, complete, and expression in Escherichia coli of cDNA for) IT 141101-72-6 141101-73-7 141101-74-8 141101-75-9 141101-76-0 141101-77-1 RL: BIOL (Biological study) (epitope of Fagales pollen allergen) ΙT 143068-37-5, Deoxyribonucleic acid (alder allergen Aln g I messenger RNA-complementary plus 3'-flanking region fragment) 143068-41-1, Deoxyribonucleic acid (birch allergen Bet v I messenger RNA-complementary plus 3'-flanking region fragment) 143068-64-8, Deoxyribonucleic acid (hazel allergen Cor a I isoform 3 messenger RNA-complementary minus terminator fragment) 143068-66-0, Deoxyribonucleic acid (hazel allergen Cor a I isoform 1 messenger RNA-complementary plus 3'-flanking region fragment) 143068-67-1, Deoxyribonucleic acid (hazel allergen Cor a I isoform 2 messenger RNA-complementary plus 3'-flanking region fragment) 143068-69-3, Deoxyribonucleic acid (hazel allergen Cor a I isoform 4 messenger RNA-complementary plus 3'-flanking region fragment)

RL: BIOL (Biological study)

```
(nucleotide sequence of and cloning in Escherichia coli of)
     143068-36-4, Deoxyribonucleic acid (alder allergen Aln g I messenger
TΥ
     RNA-complementary minus terminator fragment)
                                                     143068-40-0,
     Deoxyribonucleic acid (birch allergen Bet v I
     messenger RNA-complementary minus terminator fragment)
                                                               143068-62-6,
     Deoxyribonucleic acid (hazel allergen Cor a I isoform 1 messenger
     RNA-complementary minus terminator fragment)
                                                    143068-63-7,
     Deoxyribonucleic acid (hazel allergen Cor a I isoform 2 messenger
     RNA-complementary minus terminator fragment)
                                                    143068-65-9,
     Deoxyribonucleic acid (hazel allergen Cor a I isoform 4 messenger
     RNA-complementary minus terminator fragment)
                                                    143068-68-2,
     Deoxyribonucleic acid (hazel allergen Cor a I isoform 3 messenger
     RNA-complementary plus 3'-flanking region fragment)
     RL: PRP (Properties); BIOL (Biological study)
        (nucleotide sequence of, complete, and expression in Escherichia coli
        of)
L5
     ANSWER 24 OF 26 CAPLUS COPYRIGHT 2000 ACS
ΑN
     19,93:167338
                 CAPLUS
DN
     1/18:167338
TΙ
     Homology of two cDNAs coding for birch pollen allergens with calmodulin:
     Protein-bound calcium affects the IgE-binding capacity
     Seiberler, Susanne; Scheiner, Otto; Kraft, Dietrich; Valenta, Rudolf
ćs
     Inst. Gen. Exp. Pathol., Univ. Vienna, Vienna, A-1090, Austria
     Int. Arch. Allergy Immunol. (1992), 99(2-4), 380-1
     CODEN: IAAIEG; ISSN: 1018-2438
DT
     Journal
LΑ
     English
     15-9 (Immunochemistry)
     Section cross-reference(s): 3
AΒ
     Birch pollen is known to contain 2 well-defined allergens, Bet v I, a
     protein, which is a major allergen for 95% of the birch-pollen-allergic
     individuals, and birch profilin, identified as a novel type of plant pan
     allergen. Here, is reported the identification of 2 novel birch pollen
     allergens with a sequence homol. to calmodulin. Although both allergens
     are rare targets for patients' IgE (5-10%), they are of particular
     interest because both proteins require the native protein conformation
and
     protein-bound Ca2+ for IgE binding. Thus, for the first time an IgE
     epitope is described which is assembled by a polypeptide and a
     divalent cation, Ca2+.
ST
    birch pollen allergen epitope calcium complex; IgE binding birch
    pollen allergen calcium
ΙT
     Pollen
        (allergen from birch, IgE epitope on, calcium-dependent,
        calmodulins in relation to)
IT
    Birch
        (allergen from pollen of, IgE epitope on,
        calcium-dependent, calmodulins in relation to)
    Calmodulins
    RL: BIOL (Biological study)
        (birch pollen allergens homologous to)
ΤТ
    Allergens
    RL: BIOL (Biological study)
        (of birch pollen, IgE epitope on, calcium-dependent,
       calmodulins in relation to)
IT
    Protein sequences
        (of calcium-dependent allergen, of birch pollen)
```

```
ΙT
     Immunoglobulins
     RL: BIOL (Biological study)
        (E, birch pollen allergen binding by, calcium-dependent epitope
        in)
IT
     7440-70-2, Calcium, biological studies
     RL: BIOL (Biological study)
        (IgE epitope on birch pollen allergen dependence on)
L5
     ANSWER 25 OF 26 CAPLUS COPYRIGHT 2000 ACS
     1991:183460 CAPLUS
AN
DN
     114:183460
TI
                    v I epitopes by using murine monoclonal
     Mapping of Bet/
     antibodies
ΑŲ
     Marc-Series, I.; Boutin, Y.; Vrancken, E. R.; Hebert, J.
CS
     Unite Rech. Inflammation Immunol. Rhumatol., CHUL, Ste-Foy, PQ, G1V 4G2,
SO
     Int. Arch. Allergy Appl. Immunol. (1990), 92(3), 226-32
     COMEN: IAAAAM; ISSN: 0020-5915
DT
     Yournal
LΑ
     English
CC,
     15-2 (Immunochemistry)
     The different determinants of birch pollen exts., as shown by SDS-PAGE
     anal., range from 10 to 94 kDa. These determinants were then
     electrotransferred on nitrocellulose strips and allowed to react with
     human IgE Ab from sensitive patients in order to identify the allergenic
     determinants. Several minor (43, 35, 28 and 21 kDa) and the major (17
     kDa) allergenic determinants were identified. Murine monoclonal
     antibodies (mAb) were then produced against the major allergenic
     determinant (Bet v I) and their specificity confirmed by immunoblot. One
     of them, mAb 3F10, was used to affinity-purify the Bet v I. The purity
of
     this material was confirmed by SDS-PAGE anal. and its reactivity on
     immunoblot against human IgE ensured its biol. activity. These mAb were
     then sepd. into four families based on their pattern of reactivity with
     Bet v I. Indeed, four different epitopes on the mol. were
     identified. Binding inhibition studies using two of them (mAb 5F9 and
     8F12) suggested that the epitopes of Bet v I recognized by these
     mAb are not overlapping. Howevaer, the binding of 8H7 and 3F10 was
     partially inhibited by 5F9 and the binding of 3F10, by 8F12. These data
     suggest that those two latter epitopes are somewhat overlapping.
     The mAb 5F9 could inhibit the binding of human IgE on the
     affinity-purified Bet v I up to 40% and then shares a common idiotope
with
     human specific IgE Ab of allergic patients.
ST
     Bet V I allergen epitope; birch pollen allergen epitope
IT
     Allergens
     RL: BIOL (Biological study)
        (Bet v I, epitopes of birch pollen, mapping of, monoclonal
        antibodies for)
ΙT
        (allergen Bet v I of birch, epitopes of, mapping of,
        monoclonal antibodies for)
IΤ
     Birch
        (allergen Bet v I of pollen of, epitopes of,
        mapping of, monoclonal antibodies for)
L5
     ANSWER 26 OF 26 MEDLINE
                                                        DUPLICATE 1
ΑN
     91076141
                 MEDITNE
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91076141
ΤI
     Cross-reactivity among the pollen proteins of birch and apple trees.
ΑU
     Berrens L; van Dijk A G; Houben G F; Hagemans M L; Koers W J
     CBF Research Group, Madrid.
CS
     ALLERGIE UND IMMUNOLOGIE, (1990) 36 (3) 147-56.
SO
     Journal code: 3A4. ISSN: 0323-4398.
CY
     GERMANY: Germany, Federal Republic of
     (CLINICAL TRIAL)
DT
     Journal; Article; (JOURNAL ARTICLE)
     (RANDOMIZED CONTROLLED TRIAL)
LΑ
     English
     Priority Journals
FS
ΕM
     199103
AB
     In the spring of 1986, the pollen were collected from apple trees in full
     blossom, and were investigated for their allergenicity. The patients
     selected for study were subjects with a combined inhalant allergy to
birch
     pollen and an oral allergy to apple fruit. The apple pollen extract
     yielded about the same percentage of nondialysable substance as obtained
     from birch pollen. In contrast to the latter, UV-spectroscopy revealed no
     flavonoids adsorbed to the apple pollen proteins. Patients with a
combined
     allergy to birch pollen and apple fruit showed positive skin reactions to
     both birch and apple pollen extract. Inhibition of IgE-binding in RAST to
     birch pollen was observed by apple pollen extract at a 1000-fold lower
     potency than the homologous birch allergens.
     Immunoblotting demonstrated IgG-antibodies in birch-allergic sera
     cross-reactive with apple pollen components. It is concluded that minor
     allergenic determinants cross-reactive with birch pollen epitopes
     occur not only in the fruit, but also in the pollen of the apple tree.
CT
     Check Tags: Human
      Cross Reactions
      Fruit: IM, immunology
     *Hay Fever: IM, immunology
      Isoelectric Point
     *Pollen: IM, immunology
      Pollen: UL, ultrastructure
      Radioallergosorbent Test
      Skin Tests
      Spectrophotometry, Ultraviolet
     *Trees
=> s ipsen h
L6
             0 IPSEN H
=> s spangfort md
L7
             0 SPANGFORT MD
=> s larsen j
rs
             7 LARSEN J
=> dup remove 18
PROCESSING COMPLETED FOR L8
```

DN

=> d 19 all 1-6

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L9 ANSWER 1 OF 6 SCISEARCH COPYRIGHT 2000 ISI (R)
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AN 2000:832780 SCISEARCH

GA The Genuine Article (R) Number: 369JV

TI Ab initio calculations for elucidation of the lanosterol 14 alpha-demethylation mechanism

AU CabreraVivas B M (Reprint); Melendez F J; MartinezAguilera L M R; KubliGarfias C

CS PRIV 37 OTE 1602, COL EL MIRADOR, PUEBLA 72530, MEXICO (Reprint);
BENEMERITA UNIV AUTONOMA PUEBLA, FAC CIENCIAS QUIM, PUEBLA, MEXICO; UNIV
NACL AUTONOMA MEXICO, INST INVEST BIOMED, LAB QUIM HORMONAL, MEXICO CITY
04510, DF, MEXICO; INST MEXICANO PETR, MEXICO CITY 07730, DF, MEXICO
CYA MEXICO

SO JOURNAL OF MOLECULAR STRUCTURE-THEOCHEM, (17 NOV 2000) Vol. 532, pp. 245-256.

Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS.

ISSN: 0166-1280.

DT Article; Journal

FS PHYS

LA English

REC Reference Count: 39

AB Ab initio calculations at the RHF/6-31G\* level were performed with the SPARTAN program in order to elucidate the best pathway through which norlanosterol could be biosynthesized from lanosterol (demethylation).

Two

possible main pathways have been reported: the pathway via intermediate carboxylic acid proposed by Olson and Akhtar [J.A. Olson, M. Lindberg, K. Bloch, J. Biol. Chem. 226 (1957) 941-956; M. Akhtar, I.A. Watkinson, A.D. Rahimtula, D.C. Wilton, K.A. Munday, Biochem. J. 111 (1969) 757-761], and the pathway via intermediate formyloxy proposed by Alexander et al. [K. Alexander, M. Akhtar, R.B. Boar, J.F. McGhie, D.H.R. Barton, J. Chem.

Sec.

Chem. Commun. (1972) 383-386; R.T. Fischer, J.M. Trzaskos, R.L. Magolda, S.S. Koo, C.S, Brosz, B. Larsen, J. Biol. Chem. 266

(10) (1991) 6124-6132]. We conclude that the formyloxy pathway is more feasible than the carboxylic acid pathway based on an analysis of frontier

orbitals, hardness/softness and reactivity parameters. (C) 2000 Elsevier Science B.V. All rights reserved.

CC CHEMISTRY, PHYSICAL

ST Author Keywords: 14 alpha-demethylation; HOMO; LUMO; hardness and softness; exergonic and endergonic reactions

STP KeyWords Plus (R): 14-ALPHA-METHYL DEMETHYLASE; CHOLESTEROL-BIOSYNTHESIS; OXIDATIVE DEMETHYLATION; C-32 DEMETHYLATION; YEAST MICROSOMES; CYTOCHROME-P-450; INTERMEDIATE; ACCUMULATION

RE

Referenced Author (RAU)	Year   VOL   P  (RPY) (RVL) (R	PG)   (RWK)
	==+=====+==	====+==================================
AKHTAR M	1969  111  75	7 IBIOCHEM J
AKHTAR M	1969  9  47	3   EUR J BIOCHEM
AKHTAR M	1968    14	06 J CHEM SOC CHEM COMM
ALEXANDER K	1972    38	•

```
|1978 |82
                                   133
                                          |BIOCHEM BIOPH RES CO
AOYAMA Y
                       |1978 |85
                                   128
                                          |BIOCHEM BIOPH RES CO
AOYAMA Y
                       |1986 |134
                                  1659
                                          |BIOCHEM BIOPH RES CO
AOYAMA Y
                      |1962 |259
                                  |16
                                          | J BIOL CHEM
                      |1989 |264
AOYAMA Y
                                  |2
                                          | J BIOL CHEM
CANONICA L
                      |1968 |90
                                   |3597 |J AM CHEM SOC
CLAYTON R B
                      |1956 |218
                                  1319
                                          | J BIOL CHEM
DAWSON J H
                      |1988 |240 |433
                                         SCIENCE
EDWARDS J O
                     |1962 |84
                                   116
                                         | J AM CHEM SOC
FIECCHI A
                     |1972 |180 |147
                                         IP R LOND B
FIESER L F
                     |1959 |364 |364
                                          ISTEROIDS
FISCHER R T
                     |1991 |266 |6124 |J BIOL CHEM
FISCHER R T
                     |1989 |30
                                   |1621 |J LIPID RES
FUKUI K
                      |1982 |218 |747
                                          |SCIENCE
GAYLOR J L
                      |1963 |238
                                  |1649 |J BIOL CHEM
                     |1979 |183
GIBBONS G F
                                  1309
                                         |BIOCHEM J
GOODMAN D S
                      |1963 |238
                                  |1287 |J BIOL CHEM
GUENGERICH F P
                      |1984 |17
                                  19
                                         ACCOUNTS CHEM RES
                                   |1145 |J AM CHEM SOC
JOHNSTON J D
                      |1957 |79
KLYNE W
                      |1970 |
                                   19
                                         |QUIMICA ESTEROIDES
KUBLIGARFIAS C
                      |1996 |388
                                  135
                                         | J MOL STRUCT THEOCHE
LEHNINGER A L
                      |1995 |
                                   1254
                                         | PRINCIPIOS BIOQUIMIC
LIU H I
                      |1995 |270
                                  |10544 |J BIOL CHEM
                      |1957 |226
|1967 |89
OLSON J A
                                  |941 |J BIOL CHEM
PEARSON R G
                                        | J AM CHEM SOC
                                  11827
                     |1966 |151 |172 |SCIENCE
PEARSON R G
SCHROEPFER G J
                                  |555 |ANN REV BIOCH
|1668 |J BIOL CHEM
                      |1982 |51
SCHROEPFER G J
                      |1961 |236
SCHROEPFER G J
                      |1972 |180 |125 | P ROY SOC LOND B BIO
SHAFIEE A
                      |1986 |27
                                  11
                                         |J LIPID RES
TRZASKOS J M
                      |1984 |259
                                  |13402 |J BIOL CHEM
TRZASKOS J M
                      |1986 |261 |16937 |J BIOL CHEM
WATKINSON I A
                      |1971 |121 |131 |BIOCHEM J
WHITE A
                      |1968 |
                                  180
                                         | PRINCIPLES BIOCH
WHITE R E
                      |1980 |49
                                  1315
                                         |ANN REV BIOCH
    ANSWER 2 OF 6 SCISEARCH COPYRIGHT 2000 ISI (R)
L9
ΑN
     1998:624080 SCISEARCH
GΑ
    The Genuine Article (R) Number: 109DW
    Internal generation of waves for time-dependent mild-slope equations
    Lee C (Reprint); Suh K D
ΑU
CS
    KOREA OCEAN RES & DEV INST, COASTAL & HARBOUR ENGN DIV, ANSAN POB 29,
    SEOUL 425600, SOUTH KOREA (Reprint); SEOUL NATL UNIV, DEPT CIVIL ENGN,
    SEOUL 151742, SOUTH KOREA
CYA SOUTH KOREA
    COASTAL ENGINEERING, (JUL 1998) Vol. 34, No. 1-2, pp. 35-57.
     Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM,
    NETHERLANDS.
    ISSN: 0378-3839.
DT
    Article; Journal
FS
    ENGI
LA
    English
REC Reference Count: 21
       A technique for internal generation of waves is studied for two
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time-dependent mild-slope equation models developed by Copeland

G.J.M., 1985. A practical alternative to the mild-slope wave equation. Coastal Eng., 9, pp. 125-149] and Radder and Dingemans [Radder, A.C.,

AOYAMA Y

[Copeland,

Dingemans, M.W., 1985. Canonical equations for almost periodic, weakly nonlinear gravity waves. Wave Motion, 7, pp. 473-485]. For the Radder and Dingemans' equations, desired energy of incident waves could not be obtained from the viewpoint of mass transport which has successfully been used for the Boussinesq equations and the Copeland equations by Larsen

and

Dancy [Larsen, J., Dancy, H., 1983. Open boundaries in short wave simulations—a new approach. Coastal Eng., 7, pp. 285-297] and Madsen and Larsen [Madsen, P.A., Larsen, J., 1987. An efficient finite—difference approach to the mild—slope equation. Coastal Eng., 11, pp. 329-351], respectively. However, for both of the Copeland's and Radder and Dingemans' models, desired energy of incident waves could be obtained from the viewpoint of energy transport. Using the viewpoint

of

energy transport in the Radder and Dingemans equations, which treat random  $% \left( 1\right) =\left( 1\right) +\left( 1\right)$ 

waves of narrow frequency band properly, we could successfully generate not only monochromatic waves but also directional random waves. (C) 1998 Elsevier Science B.V. All rights reserved.

CC ENGINEERING, CIVIL; ENGINEERING, MARINE

Author Keywords: time-dependent mild-slope equations; numerical wave generation; energy transport

STP KeyWords Plus (R): LINEAR DISPERSION CHARACTERISTICS; BOUSSINESQ EQUATIONS; FORM

RE

KD				
Referenced Author	Year	VOL	PG	Referenced Work
(RAU)	(RPY)	(RVL)	(RPG)	(RWK)
=======================================	=+====+	=====+	-====	+===============
BERKHOFF J C W	1972		471	13TH P INT C COAST E
BOOIJ N	1981			811 DELFT U TECH DEP
COPELAND G J M	1985	9	125	COAST ENG
KIM T	1994	1	340	P 2J INT C COAST ENG
KIRBY J T	1984	89	745	J GEOPHYS RES OCEANS
KIRBY J T	1992	1	391	P 23 INT C COAST ENG
KOBUNE K	1986	1	80	P 5 INT OFFSH MECH A
KUBO Y	1992	!	419	P 20 INT C COAST ENG
LARSEN J	1983	7	285	COAST ENG
LEE C	1994			THESIS U DELAWARE
LEE C H	1994	6	389	J KOREAN SOC COASTAL
MADSEN P A	1987  :	11		COAST ENG
MADSEN PA	1991	15	371	COAST ENG
MADSEN P A	1992  :	18	183	COAST ENG
NISHIMURA H	1983	- 1	123	P 30 JAP C COAST ENG
NWOGU O	1993	119	618	J WATERW PORT C ASCE
OTNES R K	1978	1		APPLIED TIME SERIES
PEREGRINE D H	1967  2	27	815	J FLUID MECH
RADDER A C	1985   7	7	473	WAVE MOTION
SMITH R	1975	72	373	J FLUID MECH
YOON S B	1996  1	16	53	J KOREAN SOC CIVIL E

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L9 ANSWER 3 OF 6 MEDLINE
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DUPLICATE 1

AN 85018257 MEDLINE

DN 85018257

NC CA 23536 (NCI)

TI Mechanism of inhibition of herpesvirus growth by 2'-5'-linked trimer of 9-beta-D-xylofuranosyladenine.

AU Goswami B B; Gosselin G; Imbach J L; Sharma O K

SO VIROLOGY, (1984 Sep) 137 (2) 400-7.

```
Journal code: XEA. ISSN: 0042-6822.
CY
     United States
DT
     Journal; Article; (JOURNAL ARTICLE)
LA
     English
FS
     Priority Journals; Cancer Journals
EM
     198501
     The 2'-5'-linked trimer of 9-beta-D-xylofuranosyladenine (XyloA)3 is an
AB
     extremely potent inhibitor of growth of herpes simplex viruses 1 and 2.
     Evidence is presented that in spite of its increased stability in
     cell-free extracts (D.A. Eppstein, Y.V. Marsh, B.B. Schryver, M.A.
     Larsen, J.W. Barnett, J.P.H. Verheyden, and E.J. Prisbe,
     J. Biol. Chem. 257, 13390-13397, 1982), intact (XyloA)3 was not detected
     in Vero cells, but instead was rapidly degraded in the medium to
monomeric
     9-beta-D-xylofuranosyladenine (XyloA). The XyloA thus formed was rapidly
     taken up by cells, phosphorylated to its triphosphate, and produced
     inhibition of RNA synthesis. The observed inhibition of DNA synthesis
     (D.A. Eppstein, Y.V. Marsh, B.B. Schryver, M.A. Larsen,
     J.W. Barnett, J.P.H. Verheyden, and E.J. Prisbe, J. Biol. Chem.
     257, 13390-13397, 1982) and herpesvirus growth by (XyloA)3 (D.A.
Eppstein,
     J.W. Barnett, Y.V. Marsh, G. Gosselin, and J.L. Imbach, Nature (London)
     302, 723, 724, 1983) is most likely the result of inhibition of RNA
     synthesis by its degradation product XyloA.
CT
     Check Tags: Animal; Comparative Study; Support, Non-U.S. Gov't; Support,
     U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.
      Acyclovir: PD, pharmacology
     *Adenosine: AA, analogs & derivatives
      Adenosine: PD, pharmacology
     *Antiviral Agents: PD, pharmacology
      Cell Line
      Cercopithecus aethiops
      Kidney
     *Simplexvirus: DE, drug effects
      Simplexvirus: GD, growth & development
      Simplexvirus: GE, genetics
      Species Specificity
      Transcription, Genetic: DE, drug effects
      Vidarabine: PD, pharmacology
RN
     4185-03-9 (9-xylosyladenine); 5536-17-4 (Vidarabine); 58-61-7
(Adenosine);
     59277-89-3 (Acyclovir)
CN
     0 ((2'-5')-9-xylofuranosyladenine trimer); 0 (Antiviral Agents)
L9
     ANSWER 4 OF 6 CAPLUS COPYRIGHT 2000 ACS
ΑN
     1974:126869 CAPLUS
DN
     80:126869
TI
     Exact finite-range DWBA [distorted-wave Born analysis] analyses of
     (12C, 11B) and (12C, 13C) reaction from lead-208
ΑU
     Low, K. S.; Tamura, T.
     Cent. Nucl. Stud., Univ. Texas, Austin, Tex., USA
     Phys. Lett. B (1974), 48(4), 285-9
     CODEN: PYLBAJ
DT
     Journal
LΑ
     English
    75-1 (Nuclear Phenomena)
CC
     A rapid exact finite-range DWBA calcn. is discussed and applied to the
     anal. of (12C, 11B) and (12C, 13C) reactions on 208Pb. The calcd.
angular
                                                                        Page 50
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distributions were compared with expt. (Larsen, J. S.,
     et al., 1972); rather good agreement was obtained. Good relative
     spectroscopic factors were extd. from 209Bi and 207Pb states the abs.
     spectroscopic factors were correct to within a factor of 2 at the worst,
     and much better in general.
     carbon lead 208 reaction; boron 11 prodn carbon; carbon 13 prodn carbon;
ST
     bismuth 209 level; lead 207 level
     Nuclear energy level
IT
        (of bismuth-209 and lead-207, from carbon-12 bombardment of lead-208,
        calcn. of spectroscopic factors for)
IT
     13966-28-4, reactions
     RL: RCT (Reactant)
        (bombardment of, by carbon-12, calcn. of angular distributions of
        boron-11 and carbon-13 from)
IT
     14762-74-4P, preparation
                                14798-13-1P, preparation
     RL: PREP (Preparation)
        (from lead-208 by carbon-12 bombardment, angular distributions of,
        calcn. of)
IT
     7440-69-9, properties
     RL: PRP (Properties)
        (nuclear energy levels of bismuth-209, from carbon-12 bombardment of
        lead-208, calcn. of spectroscopic factors for)
ΙT
     14119-29-0, properties
     RL: PRP (Properties)
        (nuclear energy levels of, from carbon-12 bombardment of lead-208,
        calcn. of spectroscopic factors for)
     ANSWER 5 OF 6 CAPLUS COPYRIGHT 2000 ACS
ΑN
     1970:89610 CAPLUS
DN
     72:89610
ΤI
     Protonation of 9-ethyl-10-methylanthracene. Absence of a large
     Baker-Nathan effect in alkylarenium-ion-formation
     Brouwer, D. M.; Van Doorn, J. A.
ΑU
CS
     Kon./Shell-Lab., Shell Res. N. V., Amsterdam, Neth.
     Recl. Trav. Chim. Pays-Bas (1970), 89(1), 88-96
    CODEN: RTCPA3
DT
    Journal
LΑ
    English
CC
     22 (Physical Organic Chemistry)
GΙ
     For diagram(s), see printed CA Issue.
AΒ
     Protonation of 9-ethyl-10-methylanthracene in HF or CF3CO2H/H2O.BF3
     affords a mixt. of the 9H+- (I) and 10H+-9-ethyl-10-methylanthracenium
     ions (II). These ions differ in free energy by only 0.9-1.0 kcal/mole.
    This small difference in stability between I and II, which is probably
due
     to steric rather than electronic effects, shows that methyl and ethyl
     groups are approx. equally effective in stabilizing arenium ions. This
     result demonstrates, contrary to what was recently concluded (Arnett, E.
    M.; Larsen, J. W.; 1969) on the basis of calorimetric
    measurements of the heats of protonation of alkylbenzenes in FSO3H-SbF5,
     that there is no large Baker-Nathan effect in alkylarenium-ion formation.
    The PMR spectrum of I exhibits some remarkable features (notablyan
    unusually strong shielding of the ethyl-CH3 protons) that are assocd.
with
    the particular conformation of the (>CHEt) group in this ion and related
```

anthracenes protonation; protonation anthracenes; Baker Nathan effects

arenium ions; arenium ions Baker Nathan effects

```
ΙT
     Conjugation
        (hyper-, protonation of ethylmethylanthracene in relation to)
ΙT
     Protonation
        (of ethylmethylanthracene, hyperconjugation in relation to)
ΤТ
     27746-05-0 27746-06-1
     RL: PRP (Properties)
        (nuclear magnetic resonance of)
     19713-49-6
IT
     RL: RCT (Reactant)
        (protonation of, hyperconjugation in relation to)
L9
     ANSWER 6 OF 6 MEDLINE
ΑN
     58112777
                 MEDLINE
DN
     58112777
TI
     [].
     Jacob Kjaer-Larsen; 22/2 1921-9/5 1958.
ΑU
     PETERSEN P B
SO
     Ugeskr. laeger, (1958 May 22) 120 (21) 684-5.
LA
     Danish
FS
     OLDMEDLINE
     CLML5834-62430-424
OS
EM
     195812
     KJAER-LARSEN J A C O B
NA
=> s fagales allergen and IgE binding
L10
             2 FAGALES ALLERGEN AND IGE BINDING
=> d 110 all 1/2
L10
    ANSWER 1 OF 2 CAPLUS COPYRIGHT 2000 ACS
     1999:614141 CAPLUS
ΑN
DN
     131:241995
TI.
    Mutant recombinant allergens for use as allergy vaccines
M
    Ipsen, Hans Henrik; Spangfort, Michael Dho; Larsen, Jorgen Nedergaard
PA
    Alk-Abello A/S, Den.
    PCT Int. Appl., 77 pp.
SO
    CODEN: PIXXD2
DT
    Patent
LА
    English
IC
    ICM C12N015-29
    ICS C12N015-12; C07K014-415; C07K014-435; A61K039-35; A61K039-36
    15-9 (Immunochemistry)
    Section cross-reference(s): 3
FAN.CNT 1
    PATENT NO.
                     KIND DATE
                                           APPLICATION NO.
                            _____
                                           ______
                           19990923
PI
                     A1
                                          WO 1999-DK136
                                                            19990316
            AE, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU,
            CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM,
            HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
            LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD,
            SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU,
            ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
        RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
            ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
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CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     AU 9927147
                       A1
                            19991011
                                          AU 1999-27147
                                                             19990316
PRAI DK 1998-364
                      19980316
     WO 1999-DK136
                      19990316
     Novel recombinant allergens are disclosed. The allergens are
     non-naturally occurring mutants derived from naturally-occurring
     allergens. The overall .alpha.-carbon backbone tertiary structure is
     essentially preserved. Also disclosed are methods for prepg. such
     recombinant allergens as well as uses thereof. The invention is based on
     the idea that the mechanism of successful allergy vaccination is not an
     alteration of the ongoing Th2-type immune response, but rather a parallel
     initiation of a new Th1-type immune response involving tertiary epitope
     recognition by B-cells and antibody formation. Addnl., dominant
     IgE binding epitopes are proposed. These epitopes are
     supposed to be constituted by tertiary structure dependent coherent
     surface areas large enough to accommodate antibody binding and conserved
     among isoallergens, variants, and/or homologous allergens from related
     species. Mutant forms of Bet v 1 and Ves v 5 allergens were produced.
     The Bet v 1 mutants displayed reduced IgE binding
     although the tertiary structure of the wild-type \operatorname{Bet} \ v \ 1 allergen was
     retained. A "triple-patch mutant" of Bet v 1 was able to induce
     proliferation in T cell lines from 3 different birch pollen allergic
     patients with stimulation indexes similar to recombinant and naturally
     occurring Bet v 1.
     allergy vaccine allergen mutant B cell epitope IgE
ST
     binding; Bet v 1 allergen recombinant mutant allergy vaccine; Ves
     v 5 allergen recombinant mutant allergy vaccine
ΙT
     Epitopes
        (B cell, mutation of; mutant recombinant allergens for use as allergy
        vaccines)
ΙT
     Allergens
     RL: BPN (Biosynthetic preparation); BPR (Biological process); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC
     (Process); USES (Uses)
        (Bet v I (Betula verrucosa, I); mutant recombinant allergens for use
as
        allergy vaccines)
     Immunoglobulins
ΙT
     RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
        (E, binding of, redn. of; mutant recombinant allergens for use as
        allergy vaccines)
IΤ
     Ant (Formicidae)
        (Formicoidae; mutant recombinant allergens for use as allergy
vaccines)
     Dicotyledon (Magnoliopsida)
        (Oleales; mutant recombinant allergens for use as allergy vaccines)
TΤ
     Monocotyledon (Liliopsida)
        (Poales; mutant recombinant allergens for use as allergy vaccines)
ΙT
     Allergens
     RL: BPN (Biosynthetic preparation); BPR (Biological process); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC
     (Process); USES (Uses)
        (Ves v 5 (Vespula vulgaris, V); mutant recombinant allergens for use
as
        allergy vaccines)
IT
     Animal
     Apidae
    Asterales
```

```
Blattaria
     Cat (Felis catus)
     Dermatophagoides
     Dog (Canis familiaris)
     Fagales
     Horse (Equus caballus)
     Hymenoptera
     Pinales
     Pollen
     Urticales
     Venoms
     Wasp
        (allergens; mutant recombinant allergens for use as allergy
        vaccines)
ΙT
     Vaccines
        (allergy; mutant recombinant allergens for use as allergy vaccines)
ΙT
     Tertiary structure
        (maintenance of; mutant recombinant allergens for use as allergy
        vaccines)
ΙT
     Allergy inhibitors
        (mutant recombinant allergens for use as allergy vaccines)
IT
     Allergens
     RL: BPN (Biosynthetic preparation); BPR (Biological process); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC
     (Process); USES (Uses)
        (mutant recombinant allergens for use as allergy vaccines)
TΤ
     Protein sequences
        (of Bet v 1 and Ves v 5 mutants)
ΙT
     244065-79-0P
                    244065-81-4P
                                   244065-82-5P
                                                  244065-83-6P
                                                                  244065-84-7P
     244065-85-8P
                    244065-86-9P
                                   244065-87-0P
                                                  244065-88-1P
                                                                  244065-89-2P
     244065-90-5P
     RL: BPN (Biosynthetic preparation); BPR (Biological process); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC
     (Process); USES (Uses)
        (amino acid sequence; mutant recombinant allergens for use as allergy
        vaccines)
ΙT
     244179-41-7, PN: WO9947680 FIG: 3 unclaimed DNA
                                                       244179-50-8, PN:
     WO9947680 FIG: 3 unclaimed DNA
                                     244179-51-9, PN: WO9947680 FIG: 3
                    244179-52-0, PN: WO9947680 FIG: 3 unclaimed DNA
     unclaimed DNA
     244179-54-2, PN: WO9947680 FIG: 3 unclaimed DNA
                                                       244179-56-4, PN:
     WO9947680 FIG: 3 unclaimed DNA
                                     244179-57-5, PN: WO9947680 FIG: 3
     unclaimed DNA
                     244179-58-6, PN: WO9947680 FIG: 3 unclaimed DNA
     244179-59-7, PN: WO9947680 FIG: 3 unclaimed DNA
                                                       244179-60-0, PN:
     WO9947680 FIG: 3 unclaimed DNA
                                      244179-61-1, PN: WO9947680 FIG: 3
     unclaimed DNA
                     244179-62-2, PN: WO9947680 FIG: 3 unclaimed DNA
     244179-64-4, PN: WO9947680 FIG: 13 unclaimed DNA
                                                        244179-67-7, PN:
     WO9947680 FIG: 13 unclaimed DNA
                                       244179-68-8, PN: WO9947680 FIG: 13
     unclaimed DNA
     RL: PRP (Properties)
        (unclaimed nucleotide sequence; mutant recombinant allergens for use
as
        allergy vaccines)
RE.CNT
RE
(1) Ferreira, F; FASEB JOURNAL FOR EXPERIMENTAL BIOLOGY 1998, V12(2), P231
(2) Hoffman, D; JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY 1993, V92(5), P707
   MEDLINE
```

```
(3) Smith, A; CLINICAL AND EXPERIMENTAL ALLERGY 1997, V27(5), P593 CAPLUS
```

- (4) Spangfort, M; INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY 1997, V113(1-3), P243 CAPLUS
- (5) The Rockefeller University; WO 9733910 A 1997 CAPLUS
- (6) Wiedemann, P; JOURNAL OF BIOLOGICAL CHEMISTRY 1996, V271(47), P29915 CAPLUS
- L10 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2000 ACS
- AN 1993:232158 CAPLUS
- 118:232158 DN
- TΙ Four recombinant isoforms of Cor a I, the major allergen of hazel pollen, show different IgE-binding properties
- ΔIJ Breiteneder, Heimo; Ferreira, Fatima; Hoffmann-Sommergruber, Karin; Ebner,
  - Christof; Breitenbach, Michael; Rumpold, Helmut; Kraft, Dietrich; Scheiner, Otto
- Inst. Gen. Exp. Pathol., Univ. Vienna, Vienna, A-1090, Austria
  Eur. J. Biochem. (1993), 212(2), 355-62 CS
- SO CODEN: EJBCAI; ISSN: 0014-2956
- DT Journal
- LA English

the

- CC 15-9 (Immunochemistry)
  - Section cross-reference(s): 3, 11
- Previous studies showed that pollens from trees of the order Fagales AΒ (e.q.
  - birch, alder, hazel, and hornbeam) all contain 1 major allergen. proteins are cross-reactive among these tree species , and .apprx.95% of tree-pollen-allergic patients display IgE binding to
- these allergens. Using the reported N-terminal amino acid sequence of the
- hazel pollen allergen Cor a I, it was possible to amplify Cor-.alpha.-I cDNA by use of PCR. Four clones with cDNA inserts were isolated. All 4 clones contained an open reading frame of 477 nucleotides (159 amino acids) but differed in length for their 3'-non-coding regions. Within
- overlapping regions, the nucleotide sequence of the 3'-non-coding regions of the 4 clones were nearly identical. The open reading frames coded for different isoforms of the major hazel pollen allergen, Cor a I. The clones were designated Cor a I/5, 6, 11 and 16, resp. Comparison of the deduced amino acid sequences of these Cor a I isoforms revealed identities
  - of 96-99%. The sequence identities between the Cor a I isoforms and Bet
- I, the major birch pollen allergen, were 71-73% (80.5-83% similarity). Comparing amino acid sequences of Cor a I isoforms with the published sequences of Aln g I, the major allergen from alder, and Car b I and isoforms, the major allergen from hornbeam, 75.5-76.7% identity (83.6-85% similarity) and 83.6-89.9% sequence identity (89.3-95% similarity), resp.,
- was found. The 4 Cor a I cDNAs were subcloned into plasmid pKK223-3 and expressed in Escherichia coli as non-fusion proteins; their capacity to bind serum IgE from tree-pollen-allergic patients was investigated. The 4
  - cloned isoforms showed an apparent mol. mass of 17 kDa in SDS/PAGE, identical to the natural, pollen-derived Cor a I. IgE antibodies from tree-pollen-allergic patients reacted with all 4 recombinant isoforms. However, marked differences were noted in the IgEbinding patterns of the distinct isoforms. Furthermore, Cor a

I/11 was the only isoform recognized by the anti-(Ber v I) monoclonal antibody, BIP 1. These results demonstrate that Cor a I isoforms display different antigenic and allergenic properties, very likely due to few but significant changes in their amino acid sequences. These findings have implications for the development of reagents for diagnosis and immunotherapy for type I allergies. ST hazel pollen allergen isoform; Corylus major allergen I sequence IT Fagales (allergens of pollen of, human IgE to, hazel major allergen I isoforms reactivity for) ፐጥ Protein sequences (for allergen I isoforms of hazel) ΙT Immunoglobulins RL: BIOL (Biological study) (E, to allergen I of hazel, of humans, isoform reactivity of) ΙT Deoxyribonucleic acid sequences (complementary, for allergen I isoforms of hazel) ΙT Allergy (immediate hypersensitivity, IgE to tree pollen of humans with, hazel major allergen I isoform reactivity of) IT143066-17-5, Allergen Cor a I (hazel isoform 1) 143066-18-6, Allergen Cor a I (hazel isoform 2) 143066-19-7, Allergen Cor a I (hazel isoform 143066-20-0, Allergen Cor a I (hazel isoform 4) RL: PRP (Properties) (amino acid sequence of) => logout LOGOUT IS NOT A RECOGNIZED COMMAND The previous command name entered was not recognized by the system. For a list of commands available to you in the current file, enter "HELP COMMANDS" at an arrow prompt (=>). => ---Logging off of STN---Executing the logoff script... => LOG Y COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION FULL ESTIMATED COST 114.35 114.50 DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL ENTRY SESSION CA SUBSCRIBER PRICE -16.14 -16.14

STN INTERNATIONAL LOGOFF AT 14:06:42 ON 10 DEC 2000